EPA Registration Jacket 43813-27

Vol. 1

JANSSEN PHARMACEUTICA INC.

June 11, 2003

Mr. Marshall Swindell
Product Manager – Team 33
Regulatory Management Branch I
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

Re-Sub KL-115

SUBJECT: ECONEA™ Technical (EPA File Symbol 43813-ET)
Schedule for toxicology bridging studies

Dear Mr. Swindell:

This letter is a follow-up to my letter of March 7, 2003 to Mr. Dennis Edwards in which Janssen Pharmaceutica committed to perform additional toxicology studies with the active ingredient ECONEA Technical. We have arranged the additional testing according to the following schedule:

- Developmental –rat
  - Range-finding (4 week) study to start in July 03.
  - Definitive study to start in early September 03
  - Draft report in February 04
  - Final report in April 04

- 90-Day oral toxicity with neuropathology and 4 week recovery
  - Range-finding (4 week) study to start in July 03
  - Definitive study to start in September 03
  - Draft report in May/June 04
  - Final report in July 04

- Mutagenicity studies (*in vivo* micronucleous test & mammalian cell CHO/HGPRT mutagenicity assay)
  - Draft reports by February 04
  - Final reports in April 04

1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000

us.janssen.com

JANSSEN PHARMACEUTICA INC.

Following completion of this set of toxicology studies, an additional 2 months is planned to further develop the bridging rationale. Anticipating that the Agency will want the complete data submission at one time, and not individually as studies become available, the timing for this submission is projected to be in September/October 2004. Please advise otherwise.

I would also appreciate if you would reciprocate with an update on the progress of the ECONEA package placed into review, notably product chemistry, environmental fate, and ecological effects.

Sincerely,

Bill Goodwine

William R. Goodwine
Senior Director
Plant & Material Protection
(609) 730-2607

c: ✓ Dennis Edwards EPA-AD

1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000

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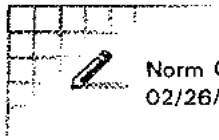
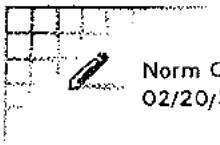


Norm Cook
02/26/200t 09:06 AM

To: Tim McMahon/DC/USEPA/US@EPA, Jonathan Chen/DC/USEPA/US@EPA, Winston Dang/DC/USEPA/US@EPA, Kathryn Montague/DC/USEPA/US@EPA, Najm Shamim/DC/USEPA/US@EPA, Nader Elkassabany/DC/USEPA/US
cc:
Subject: Please Mark on Your Calendar

Attached is background material on upcoming meeting on new antifoulant...thnx, Norm

---------- Forwarded by Norm Cook/DC/USEPA/US on 02/26/200t 09:06 AM ----------



Norm Cook
02/20/2001 07:59 AM

To: Tim McMahon/DC/USEPA/US@EPA, Jonathan Chen/DC/USEPA/US@EPA, Winston Oang/DC/USEPA/US@EPA, Kathryn Montague/DC/USEPA/US@EPA, Najm Shamim/DC/USEPA/US@EPA
cc: Nader Elkassabany/DC/USEPA/US@EPA (bcc: Norm Cook/DC/USEPA/US)
Subject: Please Mark on Your Calendar

FYI...Please plan on attending for 30 mins and mark off your calendars...we need only one person from toxicology area so let me know who will attend...if you cannot make it, pls let me know...thnx, Norm

---------- Forwarded by Norm Cook/DC/USEPA/US on 02/20/2001 07:57 AM ----------

Invitation

Chairperson:	Marshall Swindell
Start:	03/06/200t 0t:00 PM
End:	03/06/200t 04:00 PM
Description:	308U - New Chemical Pre-Application Meeting: to discuss the appropirateness of data generated to support antifoulant boat bottom use. Company will provide a list of data they have generated and the results of each study for science consideration by next Friday.

Invitees:

Detailed description:
Science Invitees need not attend for the entire time. If representatives for the following disciplines can be provided we will schedule 30 min. discussion sessions per discipline: Chemistry, Toxicology, Env. Fate, Ecological Effects, Human Exposure.
Norm, Winston, Karen Hicks, lets workout the order in which the disciples will be discussed. Please forward invite anyone else that should attend.

On 6/10/99 AD met with the company to discuss a foul-relase coating product, and a possible new chemical for antifouling use. The company was provided with a list of possible data requirements for a new antifouling active ingredient based on the then pending C9211 and Zinc omadine antifoulant applications .

A copy of the minutes of previous meeting and agenda ltr will be provided asap

Cook

Calendar Entry

○ Appointment ● Invitation ○ Event ○ Reminder ○ Anniversary

Brief description:
308U - New Chemical Pre-Application Meeting: to discuss the appropirateness of data generated to support antifoulant boat bottom use. Company will provide a list of data

Date: 03/06/2001 Time: 01:00 PM - 04:00 PM ☐ Pencil in ☐ Not for public viewing

Detailed description:
Science Invitees need not attend for the entire time. If representatives for the following disciplines can be provided we will schedule 30 min. discussion sessions per discipline: Chemistry, Toxicology, Env. Fate, Ecological Effects, Human Exposure.
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A copy of the minutes of previous meeting and agenda ltr will be provided asap

Invitations have been sent to: Dennis Edwards/DC/USEPA/US@EPA, Norm Cook/DC/USEPA/US@EPA, Winston Dang/DC/USEPA/US@EPA, Carlton Kempter/DC/USEPA/US@EPA, Eastlyn Mcintyre/DC/USEPA/US@EPA, Karen Leavy/DC/USEPA/US@EPA, Karen Hicks/DC/USEPA/US@EPA
Optional invitees: Debbie Edwards/DC/USEPA/US@EPA, Connie Welch/DC/USEPA/US@EPA
Chairperson: Marshall Swindell/DC/USEPA/US

[redacted]

The company will submit a list of data they have, along with the results on 2/23/01. This will be forwarded to you when received.

MSwindell/KLeavy

SIGMA
COATINGS

Sigma Coatings USA
P.O. Box 816
1401 Destrehan Avenue
Harvey, Louisiana 70059
(504) 347-4321
(Fax) 341-9120

Marshall Swindell
Product Manager Team 33
Regulatory Management Branch I
Antimicrobials Division
US Environmental Protection Agency
Office of Pesticide Programs
Ariel Rios Building
1200 Pennsylvania Avenue
Washington D.C. 20460

January 16, 2001

RE: Request for a Preregistration Meeting

Dear Mr. Swindell,

I am writing on behalf of Janssen Pharmaceutica and Sigma Coatings USA to request a Preregistration meeting with the Antimicrobial Division of the US EPA on the morning of March 2nd, 2001.

The background to this meeting is that Janssen Pharmaceutica has developed a unique biocidal compound for use in antifouling paints, called AF028. This material has the significant advantage of faster environmental breakdown that other biocides used in antifouling paints. Sigma Coatings has been able to formulate this biocide into an effective antifouling paint formulation, called Sigma Nexxium 20 which will be submitted for EPA registration.

At the meeting, Janssen and Sigma will be able to present the available data that has been generated on product chemistry, acute toxicity (active substance & paint formulation), chronic toxicology (including bridging data), ecotoxicity and environmental fate to support the registration of AF028. In view of the full chronic data package, the conditions requiring human exposure data need to be further discussed. Please arrange that the appropriate persons from Product Science, Risk Assessment/Science Support, and Regulatory Management Branches are present at the relevant session. We anticipate that a thorough discussion of all topics will require 3 - 3½ hours.

SIGMA COATINGS

The total number of attendees from Sigma and Janssen will be around 8 people, and we therefore request that a suitable size conference room with a projector compatible for use with PC's be available for this meeting.

If the date requested is not available, I would be happy to discuss an alternative date for this meeting. If you have any questions you can contact me at (504) 371- 0014.

Yours Sincerely,

Mike Winter
Director of R&D
Sigma Coatings USA

cc B.Goodwine - Janssen

*** Claimed confidential by submitter***

RTHERB@aol.com on 02/14/2001 04:46:03 PM

To: Marshall Swindell/DC/USEPA/US@EPA, Tony Kish/DC/USEPA/US@EPA
cc: mike.winter@sigmakalon.com
Subject: Proposed agenda for Sigma preregistration meeting March 2, 2001

CONFIDENTIAL BUSINESS INFORMATION
2/14/2001

[redacted]

hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify us immediately by telephone and return the original message to us at the above address via the U.S. Postal Service. Thank you.

*** Claimed confidential by submitter***

RTHERB@aol.com on 02/14/2001 03:41:56 PM

To: Marshall Swindell/DC/USEPA/US@EPA, Tony Kish/DC/USEPA/US@EPA
cc: mike.winter@sigmakalon.com
Subject: Information regarding requested Sigma Coatings Meeting, March 2, 2001

CONFIDENTIAL BUSINESS INFORMATION

[redacted]

FACSIMILE TRANSMISSION

****

SIGMA COATINGS USA B.V.
P.O. BOX 816
HARVEY, LOUISIANA 70059
TELEPHONE : (504) 347 4321
FAX : (504) 340 1147

****

TO: FAX NO : (703) 308 8481
COMPANY : EPA
ATTN : Tony Kish
ADDRESS :
COUNTRY :

****

FROM: NAME : Mike Winter
REF NO :
DATE : 6/23/99
PAGES : 3

****

CC: B.Herbolsheimer

****

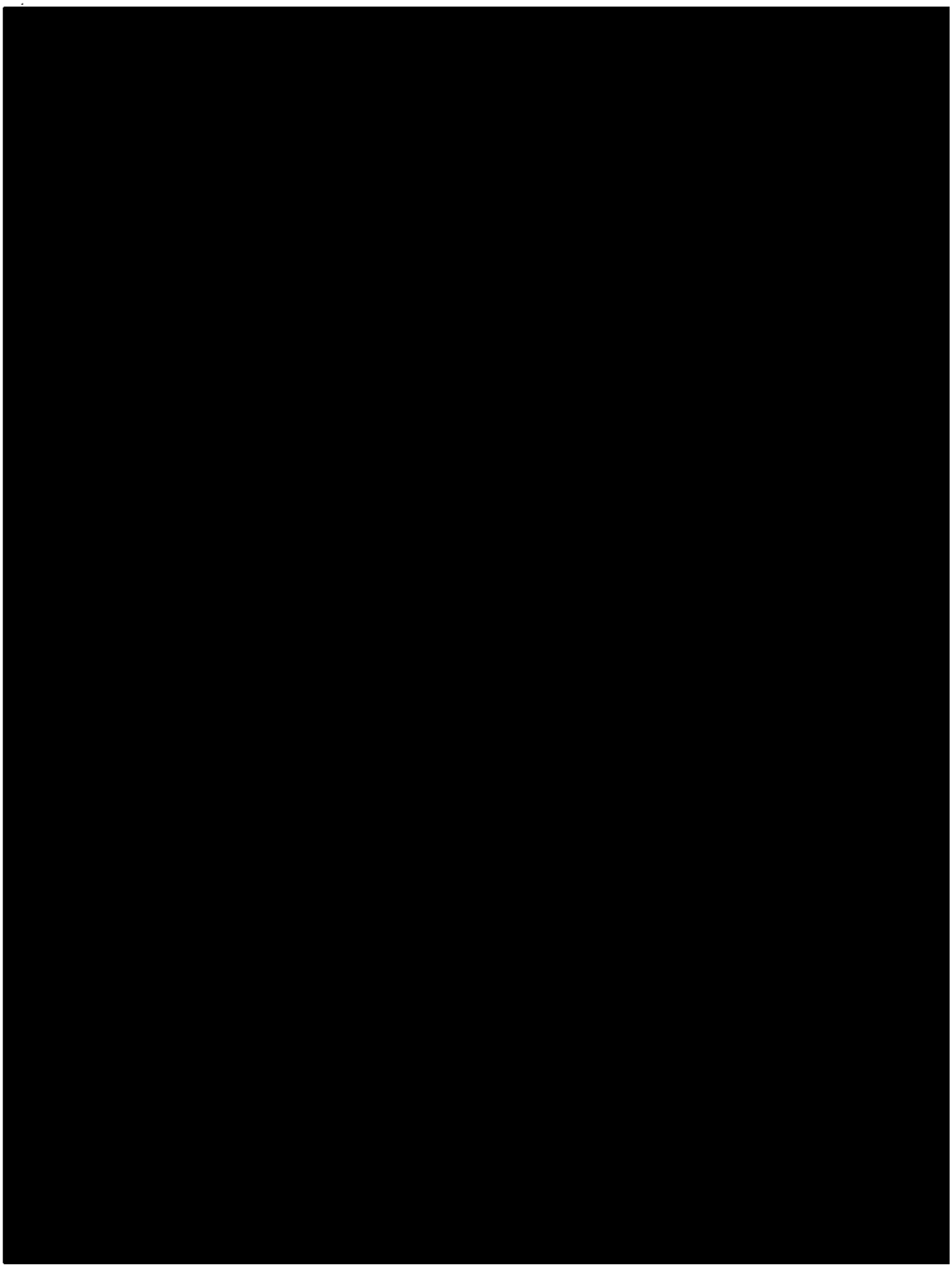
Dear Tony,

I would like to thank you for your assistance in setting up the recent Sigma Coatings/EPA meeting and for the time that you, Marshall Swindell and Martha Terry spent with us. I have attached a copy of the minutes of this meeting and I believe the correct protocol is for EPA to acknowledge receipt and acceptance of the minutes. If you have any problems or questions regarding this, please contact me at (504) 371 0014.

Yours Sincerely,

Mike Winter
Product Manager

[redacted]



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUL 07 1999

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Mike Winter
Sigma Coatings, Inc.
P.O. Box 816
Harvey, LA 70059

RE: File Symbol 11350-GU
Sigmaplane Ecol HA 5294
EPA Concurrence With Your Meeting Minutes Summary

We received your fax which summarizes the minutes of the meeting we held with you on 6/10/99 to discuss general and specific antifoulant paint questions. We concur with your minutes except for the following two comments.

1. Your blanket statement [redacted]

2. [redacted]

If you have any questions about the comments in this letter, please feel free to contact Tony Kish at 703-308-9443.

Sincerely,

Marshall Swindell,
Product Manager Team 33,
Regulatory Management Branch I
Antimicrobials Division (7510C)

*** Claimed confidential by submitter***

Sigma Coatings USA
P.O. Box 816
1401 Destrehan Ave.
Harvey, LA 70059

Attn.: Mike Winter
and
Janssen Pharmaceutica
Attn.: W. Goodwine

Subject: Pre-application Meeting For New Active Ingredient: AF028, and
New Antifoulant Paint Product: Sigma Nexxium
Meeting Held March 7, 2001

On the date referred to above members of the Antimicrobials Division (AD) held a pre-application meeting with representatives from Sigma Coatings, Janssen Pharmaceutica, and BASF Corporation. The attendees of the meeting are listed below:

USEPA/Antimicrobials Division

Marshall Swindell, Carlton Kempter, Karen P. Hicks, Jonathan Chen, Norman Cook, Kathryn Montague, Najim Shamim, Doreen Aviado, Winston Dang, Karen Leavy, and Timothy McMahon.

Company Representatives:

Nys Jan (Janssen, Belgium), Bill Goodwin (Janssen, USA), Frederick Hess (BASF, USA), Jane E. Harris (BASF, USA), Dolores A. Chiarello (BASF, USA), Mike Winter (Sigma Coatings).

The following is a description of the discussions held and decisions made during the meeting:

Administrative

The new active ingredient AF028 (aka R107894) is intended for use in antifouling paint product. The active is a metabolite of an insecticide currently registered with EPA The registered insecticide is an inactive precursor which is metabolized to form the new active ingredient. AF028 is intended to control the growth of barnacles. BASF will be manufacturing the new ai, Janssen will register the technical grade active, and Sigma Coatings will register the

end-use formula.

Sigma Coating's proposed end-use formula will also contain the active ingredient Sea Nine 211 from [redacted] to control the growth of algae.. The initial end-use application will be for use on commercial vessels, and gov., and Navy ships. Sigma may seek use on pleasure crafts at a later date. Janssen and Sigma expect to file for registration of the technical and end-use application by the fourth quarter of this calender year. The new active is currently being used in Italy, Greece, and Spain for antifoulant use (for the last year).

In preparation for the meeting the companies submitted a listing of all data they have generated in support of the new active ingredient. These studies should be submitted in support of the TGAI in addition to the missing studies indicated below.

Toxicology

The new active ingredient functions by uncoupling oxidative phosphorilation in the mitochondria of cells. The level of toxicity is directly proportional to the rate of conversion of the precursor/parent compound to the new active. The conversion rate varies between species and sex.

To support the insecticide registration, BASF has conducted a number of toxicity studies on the precursor/parent compound. The company has calculated that the toxicity of the parent compound comes from the amount of the new active which is formed from cellular metabolism. On this basis the company proposes to use the current toxicity data on file with the agency for the parent compound. They will submit a justification for such an approach and copies of the completed science reviews for their toxicity data. AD indicated that this information will be reviewed at the time the application submittal.

The companies have generated acute toxicity data on the parent compound, the new active ingredient, two of the metabolites of the new active, and the end-use paint formulation. A complete data set may not be available for each of the above. The Skin Irritation study is missing for each.

Chemistry and Environmental Fate

Data was conducted on the actual new active ingredient and has not been reviewed by the Registration Division. Janssen has a complete chemistry data set on the new active, and Sigma has chemistry on the end-use formulation.

BASF did not conduct a Bioaccumulation study as they considered it not required because the POW under environmental conditions (pH 8 and higher) is lower than 3. AD indicated that we will determine if this rationale is correct. AD prefers to have the study.

A Photolysis study was not conducted because of the calculated short half-life in water. AD indicated that we will discuss this issue in house, but that the company should submit a complete rationale for a waiver of the study.

AD indicated that a soil leaching study will be needed. The company agreed to conduct the study. Sigma indicated that they are currently developing paint leaching studies at Case Laboratories (NJ).

Fish and Wildlife

AD has determined that the following studies are missing and must be submitted: Acute LC50 Estuarine and Marine Organisms (3 species: Mysid Shrimp, Sheepshead Minnow, and Oyster); Seedling Emergence (Rice); Aquatic Plant Growth (2 species of algae: Diatoms & Bluegreen algae). The data the company has already generated, and has committed to generate should be submitted when available (see attached chart submitted by the company).

The companies raised the question of which degradates of the new active should be tested in the tests listed immediately above. I do not quite remember what decision we reached. I think the company was to submit a rationale for excluding certain degradates from testing as one degradate was of primary concern because it invariably was of the highest concentration. RASSB please verify.

Human Exposure

The companies were informed that they must submit the following information:

Technical Bulletin
Product use information (TGAI & End use products)
Application and Post-application information
Description of Human Activities

An actual human exposure study is not required at this time, but may be required after toxicity data has been submitted and reviewed. If the company intends to conduct an exposure study they should submit a testing protocol first, and consider the following areas of worker exposure for evaluation: manufacturing of the paint, application of paint, and post-application of paint.

MAY 20 2002

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

JANSSEN PHARM. RESEARCH FOUNDATION
P.O. BOX 200
1125 TRENTON-HARBOURTON ROAD
TITUSVILLE, NJ 085600200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 05/02/02. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents. If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below. These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels. The rejected studies and their deficiencies are described below.

Rejected study [01] :

* Judging from the pagination of the study, pages. 60 and 111. were omitted from the submitted copy.

Rejected study [02] :

* Judging from the pagination of the study, pages. . 71 . . . were omitted from the submitted copy.

MAY 20 2002

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

JANSSEN PHARM. RESEARCH FOUNDATION
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Rejected study [39] :

* Judging from the pagination of the study, pages. .51. . . were omitted from the submitted copy.

MAY 2 0 2002

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

JANSSEN PHARM. RESEARCH FOUNDATION
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Rejected study [65] :

* Judging from the pagination of the study, pages. . 36 . . were omitted from the submitted copy.

JANSSEN PHARMACEUTICA INC.

456740-00

April 25, 2002

Mr. Marshall Swindell
Product Manager Team 33
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

43813-ET

SUBJECT: ECONEA™ Technical (Janssen Code No. R107894)
Application for Registralion
Antimicrobial Division Priority Review to Replace TBTO by 2003

Dear Mr. Swindell:

Janssen Pharmaceutica Inc. is making an application for the registration of ECONEA™ Technical for formulation of antifouling treatment products under the general use pattern of aquatic non-crop. The USEPA Antimicrobial Division has indicated to the ACC Biocides Panel that TBTO replacement products for anti-fouling use would be given a priority for AD resources for expedited review.

Janssen is coordinating this submission with the submission by Sigma Coatings USA B.V. for end-use antifouling paints under the NEXXIUM™ brand of coatings. The regulatory contact for Sigma is Mr. Mike Winter [1-800-221-7978 (x247)].

The following administrative documents (1 copy) are provided:

Document	ECONEA Technical
Application for Pesticide Registration	X
Confidential Statement of Formula (CSF)	X
Certification with Respect to Citation of Data (Form 8570-34)	X
Data Support Matrices - Selective Method of Support (Form 8570-35)	X
Letters of Authorization for ECONEA & NEXXIUM from BASF Corporation	X
Specimen Label (6 copies)	X

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TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000

us.janssen.com

A certification statement from Inveresk Research, dated April 17, 2002, is attached to this transmittal letter indicating that the pH of the test solution for the primary eye irritation study is < 2. Consistent with Agency guidelines, this study was not performed, and the technical active substance was categorized as corrosive to eyes for labeling.

Studies submitted by reference to the BASF Corporation file (see Letter of Authorization) for EPA Registration No. 241-366 include:

Study Type	MRID
Acute oral toxicity for AC 303,268 (R107894)	43492824
Acute oral toxicity for metabolite CL 322,250	43492826
Acute oral toxicity for metabolite CL 325,195	43492827
Freshwater fish LC50 (Bluegill) for metabolite CL 325,195	44452617
Acute LC50 freshwater invertebrate for metabolite CL 325,195	44452618
Avian oral LD50 for AC303268 (R107894) – Mallard Duck	43492808
Avian oral LD50 for metabolite CL 325,195 – Mallard Duck	44452612
Avian oral LD50 for AC303268 (R107894) – Bobwhite Quail	43492809
Avian oral LD50 for metabolite CL325,195 – Bobwhite Quail	44452611
All subchronic & chronic toxicology, mutagenicity and metabolism studies	See attached BASF data matrix for product registration 241-366

Data Evaluation Records (DERs) have been submitted for all studies submitted by reference to assist the Anti-Microbial Division in their review.

Supporting data included in the ECONEA application are comprised of three (3) copies each of the following reports:

PRODUCT CHEMISTRY (40 CFR 158.155, 160, 162, 167, 170, 175, 180, 190)

Volume 1 Preliminary Analysis and Certification of Ingredient Limits for the Technical Grade of AC 303268, Report No. APBR 1212, February 7, 2002, BASF, OPPTS Draft Guideline 830.1550, 830.1700 & 830.1750.

MRID REJ (01)

Volume 2 Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303268: OPPTS 830.1600, "Description of Materials Used to Produce Product" and OPPTS 830.1620, "Description of Product Process, Report No. P-363.01, January 22, 2001, BASF, OPPTS Draft Guideline 830.1600 & 830.1620.

MRID REJ (02)

Volume 3 Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303.268: OPPTS 830.1670, "Description of the Formation of Impurities", Report No. P-364.01, February 5, 2002, BASF, OPPTS Draft Guideline 830.1670.

MRID 45673901

Volume 4 Validation of the Ion Chromatographic Method M-3417.01 to Assay for Triethylamine (TEA) in the CL 303268 Technical Grade Active Ingredient (TGAI), Report No. APBR 1130, November 3, 2000, BASF, OPPTS Draft Guideline Reference 830.1700.

MRID 45673902

Volume 5 Validation of HRGC Method M-3467.01 to Assay for CL 312264 and CL 322697 in the Technical Grade of AC 303268, Report No. APBR 1153, February 27, 2001, BASF, OPPTS Draft Guideline Reference 830.1700

MRID 45673903

Volume 6 Validation of High Performance Liquid Chromatographic Method M-3397.03 to Assay for the Minor Components in CL 303268 Technical Grade Active Ingredient, Report No. APBR 1129, January 30, 2001, BASF, OPPTS Draft Guideline Reference 830.1700.

MRID 45673904

Volume 7 Validation of the High Performance Liquid Chromatographic Method M-3408 to Assay for CL 303268 in the Technical Grade Active Ingredient (TGAI), Report No. APBR 1109, March 25, 2002, BASF, OPPTS Draft Guideline Reference 830.1700 & 830.1800.

MRID 45673905

Volume 8 R107894: Determination of the Physico-Chemical Properties (pH, pKa, and EC Tests A4, A6 and A8), Report No. 1073/41-D2141 (Janssen Report No. AGR00301), January 2001, Covance Laboratories Ltd., OPPTS Draft Guideline Reference Series 63 (158.190).

MRID 45673906

Volume 9 R107894: Determination of Physico-Chemical Properties, Report No. 1073/48-D2149 (Janssen Report No. AGR00351), July 2001, Covance Laboratories Ltd, OPPTS Draft Guideline Reference Series 63 (158.190).

MRID 45673907

ENVIRONMENTAL FATE (40 CFR 158.290)

Volume 10 Determination of the Hydrolytic Stability of [14C]-R107894, Report No. 15348, December 22, 1997, Inveresk Research, Date Requirement 161-1.

MRID 45673908

Volume 11 Supplement to Hydrolytic Stability Report No. 15348-Identification of Hydrolytic Degradation Products of [14C]-R107894, Report No. 15365, December 17, 1997, Inveresk Research, Data Requirement 161-1.

MRID 45673909

Volume 12 The Anaerobic Degradation of [14C]-R107894 in Two Water/Sediment Systems, Report No. 17832, January 12, 2000, Inveresk Research, Data Requirement 162-3.

MRID 45673910

Volume 13 The Aerobic Degradation of [14C]-R107894 in Two Water/Sediment Systems, Report No. 16787, February 15, 1999, Inveresk Research, Data Requirement 162-4.

MRID 45673911

Volume 14 Supplement to Report No. 16787-The Aerobic Degradation of R107894 in Two Water/Sediment Systems, Report No. 17802, October 19, 1999, Inveresk Research, Data Requirement 162-4.

MRID 45673912

Volume 15 Adsorption/Desorption of [14C]-R107894 in Sediments, Report No. 15715, April 7, 1998, Inveresk Research, Data Requirement 163-1.

MRID 45673913

Volume 16 Adsorption/Desorption of the Hydrolysis Products of [14C]-R107894 in Sediments, Report No. 16693, January 22, 1999, Inveresk Research, Data Requirement 163-1.

MRID 45673914

Volume 17 Justification for waiver to conduct soil leaching studies with R107894 based on existing data and pesticide assessment guidance, Report No. 13751-6131, December 13, 2001, Springborn Laboratories, Inc., Guideline Reference 163-1.

MRID ADMIN

TOXICOLOGY (40 CFR 158.340)

ACUTE TOXICOLOGY

Volume 18 R107894 Technical Acute Oral Toxicity (Fixed Dose Procedure) Test in Rats, Report No. 19839, Janssen Report No. AGR308, November 20, 2001, Inveresk Research, OPPTS Draft Guideline 870.1100.

MRID 45673915

Volume 19 R107894 Technical Acute Dermal Toxicity (LD50) Test in Rats, Report No. 19836, Janssen Report No. AGR307, November 20, 2001, Inveresk Research, OPPTS Draft Guideline 870.1200.

MRID 45673916

Volume 20 R107894 Technical Acute Inhalation Toxicity Study in Rats, Report No. 19794 (Report Amendment), October 12, 2001, Inveresk Research, OPPTS Draft Guideline 870.1300.

MRID 45673917

Volume 21 R107894 Technical Acute Dermal Irritation Test in Rabbits, Report No. 20682, Janssen Report No. AGR306, January 11, 2002, Inveresk Research, OPPTS Draft Guideline 870.2500.

MRID 45673918

Volume 22 R107894 Technical Buehler Test in Guinea Pigs for Delayed Skin Sensitization Potential, Report No. 20973, Janssen Report No. AGR304, January 17, 2002, Inveresk Research, OPPTS Draft Guideline 870.2600.

MRID 45673919

Volume 23 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Acute Oral Toxicity for AC303,630 (R107894), and metabolites CL 322,250 & CL 325,195, Guideline 81-1

MRID 45673920

SUBCHRONIC TOXICITY

Volume 24 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 82-1 (870.3100), 82-1a (870.3150), 82-1b (870.3150), 82-2 (870-3200), 82-7 (870.6200), Subchronic Toxicity.

MRID ADMIN

CHRONIC TOXICITY

Volume 25 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 83-1b (870.4100), 83-3a (870.3700), 83-3b (870.3700), 83-4 (870.3800), 83-5 (870.4300), Chronic Toxicity.

MRID ADMIN

MUTAGENICITY

Volume 26 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 84-2 (870.5100), 84-2 (870.5300), 84-2 (870.5375), 84-2 (870.5395), 84-2 (870.5550), Mutagenicity.

MRID ADMIN

METABOLISM

Volume 27 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 85-1 (870.7485), Metabolism.

MRID ADMIN

ECO-TOXICITY (40 CFR 158.490)

Parent Compound R107894

Volume 28 Acute toxicity of R107894 technical fish, *Oncorhynchus mykiss*, Report No. WE-03-220, (Janssen Rpt. No. AGR 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID 45674001

Volume 29 Acute toxicity of R107894 technical for fish, *Lepomis macrochirus*, Report No. WE-03-227, (Janssen Rpt. No. AGR 294), April 15, 2002, LISEC, OPPTS Draft Guideline No. 850.1075

MRID 45674002

Volume 30 R107894-Acute Toxicity to Sheepshead Minnow (*Cyprinodon variegatus*) Under Flow-Through Conditions, Report No. 13751.6119 (Janssen Rpt. No. AGR 368), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1075.

MRID 45674003

Volume 31 Acute toxicity of R107894 technical for *Daphnia magna*, Report No. WE-01-250 (Janssen Rpt. No. AGR 298), December 10, 2001, LISEC, OPPTS Draft Guideline 850.1010

MRID 45674004

Volume 32 R107894-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6120 (Janssen Rpt. No. AGR 365), December 3, 2001, Springborn Labs, OPPTS Draft Guideline 850.1025.

MRID 45674005

Volume 33 R107894-Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions, Report No. 13751.6118 (Janssen Rpt. No. AGR 371), October 18, 2001, Springbom Laboratories, OPPTS Draft Guideline 850.1035.

MRID 45674006

Volume 34 R107894-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6128 (Janssen Rpt. No. AGR 383), November 6, 2001, Springbom Labs, OPPTS Draft Guideline 850.1400

MRID 45674007

Volume 35 *Daphnia magna* reproduction test of R107894 technical, Report No. WE-02-051, (Janssen Rpt. No. AGR 292), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674008

Volume 36 R107894-Life-Cycle Toxicity Test with Mysids *(Americamysis bahia)*, Report No. 13751.6107 (Janssen Rpt. No. AGR336), July 9, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1350

MRID 45674009

Volume 37 R107894-Toxicity to Amphipods *(Hyalella azteca)* During a 10-Day Sediment Exposure, Report No. 13751.6105 (Janssen Rpt. No. AGR 340), July 5, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45674010

Volume 38 R107894-Toxicity to Marine Amphipods *(Leptocheirus plumulosus)* During a 10-Day Sediment Exposure, Report No. 13751.6106 (Janssen Rpt. No. AGR 332), July 6, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674011

Volume 39 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Satisfying Avian LD50 Data Requirements for Mallard Ducks and Bobwhite Quail for AC303,630 (R107894 and Metabolite CL 325,195), Guideline 71-1

MRID RET (39)

Metabolite CL 325,195

Volume 40 Acute toxicity of CL 325,195 for fish, *Oncorhynchus mykiss*, Report No. WE-03-219, (Janssen Rpt. No. AGR 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID 45674012

Volume 41 CL 325,195 - Acute Toxicity to Sheepshead Minnow (Cyprinodon variegatus) Under Flow-Through Conditions, Report No. 13751.6125 (Janssen Rpt. No. AGR 366), December 10, 2001, Springborn Laboratories. OPPTS Draft Guideline 850.1075.

MRID 45674013

Volume 42 CL325,195-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6126 (Janssen Rpt. No. AGR363), December 13, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1025.

MRID 45674014

Volume 43 CL325,195-Acute Toxicity to Mysids (Americamysis bahia) Under Flow-Through Conditions, Report No. 13751.6124 (Janssen Rpt. No. AGR 369), November 20, 2001, Springborn Laboratories, FIFRA Guideline Reference Number 72-3, OPPTS Draft Guideline 850.1035.

MRID 45674015

Volume 44 Fish, Early-life Stage Toxicity Test of CL 325,195 *(Danio rerio)*, Report No. WE-05-003 (Janssen Rpt. No. AGR 290), February 22, 2002, LISEC, OPPTS Draft Guideline 850.1400.

MRID 45674016

Volume 45 CL 325,195-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6130 (Janssen Rpt. No. AGR384), December 13, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1400

MRID 45674017

Volume 46 *Daphnia magna* reproduction test of CL 325,195, Report No. WE-02-050 (Janssen Rpt. No. AGR292), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674018

Volume 47 CL 325,195-Toxicity to Amphipods *(Hyalella azteca)* During a 10-Day Sediment Exposure, Report No. 13751.6116 (Janssen Rpt. No. AGR 343), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45674019

Volume 48 CL 325,195-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6117 (Janssen Rpt. No. AGR 335), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674020

Volume 49 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Satisfying Aquatic Acute LC50 Toxicity Data Requirements for Bluegill and *Daphnia magna* for Metabolite CL325,195, Guideline 72-1 & 72-2

MRID 45674021

Metabolite CL 322,250

Volume 50 Acute toxicity of CL 322,250 for fish, *Oncorhynchus mykiss*, Report No. WE-03-221 (Janssen Rpt. No. 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID 45674022

Volume 51 Acute toxicity of CL 322,250 for fish, *Lepomis macrochirus*, Report No. WE-03-228 (Janssen Rpt. No. AGR294), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1075

MRID 45674023

Volume 52 CL 322,250 - Acute Toxicity to Sheepshead Minnow (Cyprinodon variegatus) Under Flow-Through Conditions, Report No. 13751.6122 (Janssen Rpt. No. AGR 367), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1075.

MRID 45674101

Volume 53 Acute toxicity of CL 322,250 for *Daphnia magna*, Report No. WE-01-251 (Janssen Rpt. No. AGR 298), December 7, 2001, LISEC, OPPTS Draft Guideline 850.1010

MRID 45674102

Volume 54 CL322,250-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6123 (Janssen Rpt. No. AGR 364), December 10, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1025.

MRID 45674103

Volume 55 CL 322,250 - Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions, Report No. 13751.6121 (Janssen Rpt. No. AGR 370), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1035.

MRID 45674104

Volume 56 Fish, Early-life Stage Toxicity Test of CL 322,250 *(Danio rerio)*, Report No. WE-05-005 (Janssen Report No. AGR 290), February 22, 2002, LISEC, OPPTS Draft Guideline 850.1400.

MRID 45674105

Volume 57 CL 322,250-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6129 (Janssen Rpt. No. AGR 385), November 6, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1400

MRID 45674106

Volume 58 *Daphnia magna* reproduction test of CL 322,250, Report No. WE-02-052, (Janssen Rpt. No. AGR 292), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674107

Volume 59 CL 322,250-Toxicity to Amphipods (*Hyalella azateca*) During a 10-Day Sediment Exposure, Report No. 13751.6109 (Janssen Rpt. No. AGR 341), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45674108

Volume 60 CL 322,250 - Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6110 (Janssen Rpt. No. AGR 333), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674109

Metabolite CL 322,248

Volume 61 Acute toxicity of CL 322,248 for fish, *Oncorhynchus mykiss*, Report No. WE-03-223, (Janssen Rpt. No. AGR296), December 10, 2001, LISEC, OPPTS Draft Guideline 850.1075

MRID 45674110

Volume 62 Acute toxicity of CL 322,248 for fish, *Lepomis machrochirus*, Report No. WE-03-229, (Janssen Rpt. No. AGR294), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1075

MRID 45674111

Volume 63 Acute toxicity of CL 322,248 for *Daphnia magna*, Report No. WE-01-263, (Janssen Rpt. No. AGR 298), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1010

MRID 45674112

Volume 64 *Daphnia magna* reproduction test of CL 322,248, Report No. WE-02-054 (Janssen Rpt. No. AGR 292), February 15, 2002. LISEC, OPPTS Draft Guideline 850.1300

MRID 45674113

Volume 65 CL 322,248 - Toxicity to Amphipods (*Hyalella azateca*) During a 10-Day Sediment Exposure, Report No. 13751.6112 (Janssen Rpt. No. AGR 342), October 11, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID REJ (65)

Volume 66 CL 322,248-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6113 (Janssen Rpt. No. AGR 334), October 11, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674114

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Parent Compound R107894

Volume 67 R107894-Determination of Effects on Seedling Emergence of Rice (*Oryza sativa*), Report No. 13751.6127 (Janssen Rpt. No. AGR362), October 23, 2001, Springborn Labs, OPPTS Draft Guidelines 850.4100 and 850.4225.

MRID 45674115

Volume 68 R107894-Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6104, (Janssen Rpt. No. AGR 337), April 24, 2001,Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674116

Volume 69 Alga, growth inhibition test effect of R107894 technical on the growth of *Raphidocelis subcapitata*, Report No. WE-06-261 (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674117

Volume 70 Alga, growth inhibition test effect of R107894 technical on the growth of *Skeletonema costatum*, Report No. WE-06-270 (Janssen Rpt. No. AGR 307), April 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID 45674118

Metabolite CL 325,195

Volume 71 CL 325,195 - Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6115 (Janssen Rpt. No. AGR 344), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674119

Volume 72 Alga, growth inhibition test effect of CL 325,195 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-260, (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674120

Volume 73 Alga, growth inhibition test effect of CL 325,195 on the growth of *Skeletonema costatum*, Report No. WE-06-269,(Janssen Rpt. No. AGR 309), February 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID 45674121

Metabolite CL 322,250

Volume 74 CL 322,250-Toxicity to Duckweed, *Lemna gibba,* Report No. 13751.6108 (Janssen Rpt. No. AGR 338), October 12, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674122

Volume 75 Alga, growth inhibition test effect of CL 322,250 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-262 (Janssen Report No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674123

Volume 76 Alga, growth inhibition test effect of CL 322,250 on the growth of *Skeletonema costatum*, Report No. WE-06-271, (Janssen Rpt. No. 309), February 15, 2002, LISEC, OPPTS Data Guideline 850.5400

MRID 45674124

Metabolite CL 322,248

Volume 77 CL 322,248 - Toxicity to Duckweed, *Lemna gibba* Report No. 13751.6111 (Janssen Rpt. No. AGR 339), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674125

Volume 78 Alga, growth inhibition test effect of CL 322,248 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-266 (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Data Guideline 850.5400.

MRID 45674126

Volume 79 Alga, growth inhibition test effect of CL 322,248 on the growth of *Skeletonema costatum*, Report No. WE-06-272, (Janssen Rpt. No. AGR 309), February 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID 45674127

OCCUPATIONAL EXPOSURE

Volume 80 Screening level occupational exposure assessments for R107894 (CL303268) as an anti-foulant in paint applied to underwater hulls, EXP Project No. 47101, EXP Report No. 02001, January 11, 2002, EXP Corporation, OPPTS Draft Guideline Series 875.

MRID 45674128

Please consider assigning priority review status to this action since it satisfies the criteria as a TBTO replacement for anti-fouling use; TBTO will no longer be allowed by the International Maritime Organization (IMO) after 2003. The USEPA Antimicrobial Division has identified TBTO anti-fouling replacement products as a priority for receiving a high level of EPA resources in 2002-03 work plan.

Please contact me directly on any matters relating to this registration application. I can be reached by phone at 609-730-2607.

Sincerely,

Bill Goodwine

William R. Goodwine
Director
Plant & Material Protection Division

Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com

Administrative Materials

MAY 2 0 2002

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

JANSSEN PHARM. RESEARCH FOUNDATION
P.O. BOX 200
1125 TRENTON-HARBOURTON ROAD
TITUSVILLE, NJ 085600200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 05/02/02. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents. If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below. These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels. The rejected studies and their deficiencies are described below.

Rejected study [01] :

* Judging from the pagination of the study, pages. 60 and 111 were omitted from the submitted copy.

Rejected study [02] :

* Judging from the pagination of the study, pages. . 71 . . . were omitted from the submitted copy.

Rejected study [39] :

* Judging from the pagination of the study, pages. . . 51 . . were omitted from the submitted copy.

Rejected study [65] :

* Judging from the pagination of the study, pages. . 36 . . were omitted from the submitted copy.

JANSSEN PHARMACEUTICA INC.

456739-00

April 25, 2002

Mr. Marshall Swindell
Product Manager Team 33
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

43813-ET

SUBJECT: ECONEA™ Technical (Janssen Code No. R107894)
Application for Registration
Antimicrobial Division Priority Review to Replace TBTO by 2003

Dear Mr. Swindell:

Janssen Pharmaceutica Inc. is making an application for the registration of ECONEA™ Technical for formulation of antifouling treatment products under the general use pattern of aquatic non-crop. The USEPA Antimicrobial Division has indicated to the ACC Biocides Panel that TBTO replacement products for anti-fouling use would be given a priority for AD resources for expedited review.

Janssen is coordinating this submission with the submission by Sigma Coatings USA B.V. for end-use antifouling paints under the NEXXIUM™ brand of coatings. The regulatory contact for Sigma is Mr. Mike Winter [1-800-221-7978 (x247)].

The following administrative documents (1 copy) are provided:

Document	ECONEA Technical
Application for Pesticide Registration	X
Confidential Statement of Formula (CSF)	X
Certification with Respect to Citation of Data (Form 8570-34)	X
Data Support Matrices - Selective Method of Support (Form 8570-35)	X
Letters of Authorization for ECONEA & NEXXIUM from BASF Corporation	X
Specimen Label (6 copies)	X

1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000

us.janssen.com

A certification statement from Inveresk Research, dated April 17, 2002, is attached to this transmittal letter indicating that the pH of the test solution for the primary eye irritation study is < 2. Consistent with Agency guidelines, this study was not performed, and the technical active substance was categorized as corrosive to eyes for labeling.

Studies submitted by reference to the BASF Corporation file (see Letter of Authorization) for EPA Registration No. 241-366 include:

Study Type	MRID
Acute oral toxicity for AC 303,268 (R107894)	43492824
Acute oral toxicity for metabolite CL 322,250	43492826
Acute oral toxicity for metabolite CL 325,195	43492827
Freshwater fish LC50 (Bluegill) for metabolite CL 325,195	44452617
Acute LC50 freshwater invertebrate for metabolite CL 325,195	44452618
Avian oral LD50 for AC303268 (R107894) – Mallard Duck	43492808
Avian oral LD50 for metabolite CL 325,195 – Mallard Duck	44452612
Avian oral LD50 for AC303268 (R107894) – Bobwhite Quail	43492809
Avian oral LD50 for metabolite CL325,195 – Bobwhite Quail	44452611
All subchronic & chronic toxicology, mutagenicity and metabolism studies	See attached BASF data matrix for product registration 241-366

Data Evaluation Records (DERs) have been submitted for all studies submitted by reference to assist the Anti-Microbial Division in their review.

Supporting data included in the ECONEA application are comprised of three (3) copies each of the following reports:

PRODUCT CHEMISTRY (40 CFR 158.155, 160, 162, 167, 170, 175, 180, 190)

Volume 1 Preliminary Analysis and Certification of Ingredient Limits for the Technical Grade of AC 303268, Report No. APBR 1212, February 7, 2002, BASF, OPPTS Draft Guideline 830.1550, 830.1700 & 830.1750.

MRID REJ (01)

Volume 2 Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303268: OPPTS 830.1600, "Description of Materials Used to Produce Product" and OPPTS 830.1620, "Description of Product Process, Report No. P-363.01, January 22, 2001, BASF, OPPTS Draft Guideline 830.1600 & 830.1620.

MRID REJ (02)

Volume 3 Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303.268: OPPTS 830.1670, "Description of the Formation of Impurities", Report No. P-364.01, February 5, 2002, BASF, OPPTS Draft Guideline 830.1670.

MRID 45673901

Volume 4 Validation of the Ion Chromatographic Method M-3417.01 to Assay for Triethylamine (TEA) in the CL 303268 Technical Grade Active Ingredient (TGAI), Report No. APBR 1130, November 3, 2000, BASF, OPPTS Draft Guideline Reference 830.1700.

MRID 45673902

Volume 5 Validation of HRGC Method M-3467.01 to Assay for CL 312264 and CL 322697 in the Technical Grade of AC 303268, Report No. APBR 1153, February 27, 2001, BASF, OPPTS Draft Guideline Reference 830.1700

MRID 45673903

Volume 6 Validation of High Performance Liquid Chromatographic Method M-3397.03 to Assay for the Minor Components in CL 303268 Technical Grade Active Ingredient, Report No. APBR 1129, January 30, 2001, BASF, OPPTS Draft Guideline Reference 830.1700.

MRID 45673904

Volume 7 Validation of the High Performance Liquid Chromatographic Method M-3408.to Assay for CL 303268 in the Technical Grade Active Ingredient (TGAI), Report No. APBR 1109, March 25, 2002, BASF, OPPTS Draft Guideline Reference 830.1700 & 830.1800.

MRID 45673905

Volume 8 R107894: Determination of the Physico-Chemical Properties (pH, pKa, and EC Tests A4, A6 and A8), Report No. 1073/41-D2141 (Janssen Report No. AGR00301), January 2001, Covance Laboratories Ltd., OPPTS Draft Guideline Reference Series 63 (158.190).

MRID 45673906

Volume 9 R107894: Determination of Physico-Chemical Properties, Report No. 1073/48-D2149 (Janssen Report No. AGR00351), July 2001, Covance Laboratories Ltd, OPPTS Draft Guideline Reference Series 63 (158.190).

MRID 45673907

ENVIRONMENTAL FATE (40 CFR 158.290)

Volume 10 Determination of the Hydrolytic Stability of [14C]-R107894, Report No. 15348, December 22, 1997, Inveresk Research, Date Requirement 161-1.

MRID 45673908

Volume 11 Supplement to Hydrolytic Stability Report No. 15348-Identification of Hydrolytic Degradation Products of [14C]-R107894, Report No. 15365, December 17, 1997, Inveresk Research, Data Requirement 161-1.

MRID 45673909

Volume 12 The Anaerobic Degradation of [14C]-R107894 in Two Water/Sediment Systems, Report No. 17832, January 12, 2000, Inveresk Research, Data Requirement 162-3.

MRID 45673910

Volume 13 The Aerobic Degradation of [14C]-R107894 in Two Water/Sediment Systems, Report No. 16787, February 15, 1999, Inveresk Research, Data Requirement 162-4.

MRID 45673911

Volume 14 Supplement to Report No. 16787-The Aerobic Degradation of R107894 in Two Water/Sediment Systems, Report No. 17802, October 19, 1999, Inveresk Research, Data Requirement 162-4.

MRID 45673912

Volume 15 Adsorption/Desorption of [14C]-R107894 in Sediments, Report No. 15715, April 7, 1998, Inveresk Research, Data Requirement 163-1.

MRID 45673913

Volume 16 Adsorption/Desorption of the Hydrolysis Products of [14C]-R107894 in Sediments, Report No. 16693, January 22, 1999, Inveresk Research, Data Requirement 163-1.

MRID 45673914

Volume 17 Justification for waiver to conduct soil leaching studies with R107894 based on existing data and pesticide assessment guidance, Report No. 13751-6131, December 13, 2001, Springborn Laboratories, Inc., Guideline Reference 163-1.

MRID ADMIN

TOXICOLOGY (40 CFR 158.340)

ACUTE TOXICOLOGY

Volume 18 R107894 Technical Acute Oral Toxicity (Fixed Dose Procedure) Test in Rats, Report No. 19839, Janssen Report No. AGR308, November 20, 2001, Inveresk Research, OPPTS Draft Guideline 870.1100.

MRID 45673915

Volume 19 R107894 Technical Acute Dermal Toxicity (LD50) Test in Rats, Report No. 19836, Janssen Report No. AGR307, November 20, 2001, Inveresk Research, OPPTS Draft Guideline 870.1200.

MRID 45673916

Volume 20 R107894 Technical Acute Inhalation Toxicity Study in Rats, Report No. 19794 (Report Amendment), October 12, 2001, Inveresk Research, OPPTS Draft Guideline 870.1300.

MRID 45673917

Volume 21 R107894 Technical Acute Dermal Irritation Test in Rabbits, Report No. 20682, Janssen Report No. AGR306, January 11, 2002, Inveresk Research, OPPTS Draft Guideline 870.2500.

MRID 45673918

Volume 22 R107894 Technical Buehler Test in Guinea Pigs for Delayed Skin Sensitization Potential, Report No. 20973, Janssen Report No. AGR304, January 17, 2002, Inveresk Research, OPPTS Draft Guideline 870.2600.

MRID 45673919

Volume 23 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Acute Oral Toxicity for AC303,630 (R107894), and metabolites CL 322,250 & CL 325,195, Guideline 81-1

MRID 45673920

SUBCHRONIC TOXICITY

Volume 24 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 82-1 (870.3100), 82-1a (870.3150), 82-1b (870.3150), 82-2 (870-3200), 82-7 (870.6200), Subchronic Toxicity.

MRID ADMIN

CHRONIC TOXICITY

Volume 25 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 83-1b (870.4100), 83-3a (870.3700), 83-3b (870.3700), 83-4 (870.3800), 83-5 (870.4300), Chronic Toxicity.

MRID ADMIN

MUTAGENICITY

Volume 26 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 84-2 (870.5100), 84-2 (870.5300), 84-2 (870.5375), 84-2 (870.5395), 84-2 (870.5550), Mutagenicity.

MRID ADMIN

METABOLISM

Volume 27 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 85-1 (870.7485), Metabolism.

MRID ADMIN

ECO-TOXICITY (40 CFR 158.490)

Parent Compound R107894

Volume 28 Acute toxicity of R107894 technical fish, *Oncorhynchus mykiss*, Report No. WE-03-220, (Janssen Rpt. No. AGR 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID 45674001

Volume 29 Acute toxicity of R107894 technical for fish, *Lepomis macrochirus*, Report No. WE-03-227, (Janssen Rpt. No. AGR 294), April 15, 2002, LISEC, OPPTS Draft Guideline No. 850.1075

MRID 45674002

Volume 30 R107894-Acute Toxicity to Sheepshead Minnow (*Cyprinodon variegatus*) Under Flow-Through Conditions, Report No. 13751.6119 (Janssen Rpt. No. AGR 368), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1075.

MRID 45674003

Volume 31 Acute toxicity of R107894 technical for *Daphnia magna*, Report No. WE-01-250 (Janssen Rpt. No. AGR 298), December 10, 2001, LISEC, OPPTS Draft Guideline 850.1010

MRID 45674004

Volume 32 R107894-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6120 (Janssen Rpt. No. AGR 365), December 3, 2001, Springborn Labs, OPPTS Draft Guideline 850.1025.

MRID 45674005

Volume 33 R107894-Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions, Report No. 13751.6118 (Janssen Rpt. No. AGR 371), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1035.

MRID 45674006

Volume 34 R107894-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6128 (Janssen Rpt. No. AGR 383), November 6, 2001, Springborn Labs, OPPTS Draft Guideline 850.1400

MRID 45674007

Volume 35 *Daphnia magna* reproduction test of R107894 technical, Report No. WE-02-051, (Janssen Rpt. No. AGR 292), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674008

Volume 36 R107894-Life-Cycle Toxicity Test with Mysids *(Americamysis bahia)*, Report No. 13751.6107 (Janssen Rpt. No. AGR336), July 9, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1350

MRID 45674009

Volume 37 R107894-Toxicity to Amphipods *(Hyalella azteca)* During a 10-Day Sediment Exposure, Report No. 13751.6105 (Janssen Rpt. No. AGR 340), July 5, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45674010

Volume 38 R107894-Toxicity to Marine Amphipods *(Leptocheirus plumulosus)* During a 10-Day Sediment Exposure, Report No. 13751.6106 (Janssen Rpt. No. AGR 332), July 6, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674011

Volume 39 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Satisfying Avian LD50 Data Requirements for Mallard Ducks and Bobwhite Quail for AC303,630 (R107894 and Metabolite CL 325,195), Guideline 71-1

MRID RET (39)

Metabolite CL 325,195

Volume 40 Acute toxicity of CL 325,195 for fish, *Oncorhynchus mykiss*, Report No. WE-03-219, (Janssen Rpt. No. AGR 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID 45674012

Volume 41 CL 325,195 - Acute Toxicity to Sheepshead Minnow (Cyprinodon variegatus) Under Flow-Through Conditions, Report No. 13751.6125 (Janssen Rpt. No. AGR 366), December 10, 2001, Springborn Laboratories. OPPTS Draft Guideline 850.1075.

MRID 45674013

Volume 42 CL325,195-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6126 (Janssen Rpt. No. AGR363), December 13, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1025.

MRID 45674014

Volume 43 CL325,195-Acute Toxicity to Mysids (Americamysis bahia) Under Flow-Through Conditions, Report No. 13751.6124 (Janssen Rpt. No. AGR 369), November 20, 2001, Springborn Laboratories, FIFRA Guideline Reference Number 72-3, OPPTS Draft Guideline 850.1035.

MRID 45674015

Volume 44 Fish, Early-life Stage Toxicity Test of CL 325,195 *(Danio rerio)*, Report No. WE-05-003 (Janssen Rpt. No. AGR 290), February 22, 2002, LISEC, OPPTS Draft Guideline 850.1400.

MRID 45674016

Volume 45 CL 325,195-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6130 (Janssen Rpt. No. AGR384), December 13, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1400

MRID 45674017

Volume 46 *Daphnia magna* reproduction test of CL 325,195, Report No. WE-02-050 (Janssen Rpt. No. AGR292), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674018

Volume 47 CL 325,195-Toxicity to Amphipods *(Hyalella azteca)* During a 10-Day Sediment Exposure, Report No. 13751.6116 (Janssen Rpt. No. AGR 343), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45674019

Volume 48 CL 325,195-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6117 (Janssen Rpt. No. AGR 335), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674020

Volume 49 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Satisfying Aquatic Acute LC50 Toxicity Data Requirements for Bluegill and *Daphnia magna* for Metabolite CL325,195, Guideline 72-1 & 72-2

MRID 45674021

Metabolite CL 322,250

Volume 50 Acute toxicity of CL 322,250 for fish, *Oncorhynchus mykiss*, Report No. WE-03-221 (Janssen Rpt. No. 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID 45674022

Volume 51 Acute toxicity of CL 322,250 for fish, *Lepomis macrochirus*, Report No. WE-03-228 (Janssen Rpt. No. AGR294), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1075

MRID 45674023

Volume 52 CL 322,250 - Acute Toxicity to Sheepshead Minnow (Cyprinodon variegatus) Under Flow-Through Conditions, Report No. 13751.6122 (Janssen Rpt. No. AGR 367), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1075.

MRID 45674101

Volume 53 Acute toxicity of CL 322,250 for *Daphnia magna*, Report No. WE-01-251 (Janssen Rpt. No. AGR 298), December 7, 2001, LISEC, OPPTS Draft Guideline 850.1010

MRID 45674102

Volume 54 CL322,250-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6123 (Janssen Rpt. No. AGR 364), December 10, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1025.

MRID 45674103

Volume 55 CL 322,250 - Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions, Report No. 13751.6121 (Janssen Rpt. No. AGR 370), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1035.

MRID 45674104

Volume 56 Fish, Early-life Stage Toxicity Test of CL 322,250 *(Danio rerio)*, Report No. WE-05-005 (Janssen Report No. AGR 290), February 22, 2002, LISEC, OPPTS Draft Guideline 850.1400.

MRID 45674105

Volume 57 CL 322,250-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6129 (Janssen Rpt. No. AGR 385), November 6, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1400

MRID 45674106

Volume 58 *Daphnia magna* reproduction test of CL 322,250, Report No. WE-02-052, (Janssen Rpt. No. AGR 292), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674107

Volume 59 CL 322,250-Toxicity to Amphipods (*Hyalella azateca*) During a 10-Day Sediment Exposure, Report No. 13751.6109 (Janssen Rpt. No. AGR 341), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45674108

Volume 60 CL 322,250 - Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6110 (Janssen Rpt. No. AGR 333), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674109

Metabolite CL 322,248

Volume 61 Acute toxicity of CL 322,248 for fish, *Oncorhynchus mykiss*, Report No. WE-03-223, (Janssen Rpt. No. AGR296), December 10, 2001, LISEC, OPPTS Draft Guideline 850.1075

MRID 45674110

Volume 62 Acute toxicity of CL 322,248 for fish, *Lepomis machrochirus*, Report No. WE-03-229, (Janssen Rpt. No. AGR294), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1075

MRID 45674111

Volume 63 Acute toxicity of CL 322,248 for *Daphnia magna*, Report No. WE-01-263, (Janssen Rpt. No. AGR 298), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1010

MRID 45674112

Volume 64 *Daphnia magna* reproduction test of CL 322,248, Report No. WE-02-054 (Janssen Rpt. No. AGR 292), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674113

Volume 65 CL 322,248 - Toxicity to Amphipods (*Hyalella azateca*) During a 10-Day Sediment Exposure, Report No. 13751.6112 (Janssen Rpt. No. AGR 342), October 11, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID REJ (65)

Volume 66 CL 322,248-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6113 (Janssen Rpt. No. AGR 334), October 11, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674114

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Parent Compound R107894

Volume 67 R107894-Determination of Effects on Seedling Emergence of Rice (*Oryza sativa*), Report No. 13751.6127 (Janssen Rpt. No. AGR362), October 23, 2001, Springborn Labs, OPPTS Draft Guidelines 850.4100 and 850.4225.

MRID 45674115

Volume 68 R107894-Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6104, (Janssen Rpt. No. AGR 337), April 24, 2001,Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674116

Volume 69 Alga, growth inhibition test effect of R107894 technical on the growth of *Raphidocelis subcapitata*, Report No. WE-06-261 (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674117

Volume 70 Alga, growth inhibition test effect of R107894 technical on the growth of *Skeletonema costatum*, Report No. WE-06-270 (Janssen Rpt. No. AGR 307), April 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID 45674118

Metabolite CL 325,195

Volume 71 CL 325,195 - Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6115 (Janssen Rpt. No. AGR 344), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674119

Volume 72 Alga, growth inhibition test effect of CL 325,195 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-260, (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674120

Volume 73 Alga, growth inhibition test effect of CL 325,195 on the growth of *Skeletonema costatum*, Report No. WE-06-269,(Janssen Rpt. No. AGR 309), February 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID 45674121

Metabolite CL 322,250

Volume 74 CL 322,250-Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6108 (Janssen Rpt. No. AGR 338), October 12, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674122

Volume 75 Alga, growth inhibition test effect of CL 322,250 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-262 (Janssen Report No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674123

Volume 76 Alga, growth inhibition test effect of CL 322,250 on the growth of *Skeletonema costatum*, Report No. WE-06-271, (Janssen Rpt. No. 309), February 15, 2002, LISEC, OPPTS Data Guideline 850.5400

MRID 45674124

Metabolite CL 322,248

Volume 77 CL 322,248 - Toxicity to Duckweed, *Lemna gibba* Report No. 13751.6111 (Janssen Rpt. No. AGR 339), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674125

Volume 78 Alga, growth inhibition test effect of CL 322,248 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-266 (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Data Guideline 850.5400.

MRID 45674126

Volume 79 Alga, growth inhibition test effect of CL 322,248 on the growth of *Skeletonema costatum*, Report No. WE-06-272, (Janssen Rpt. No. AGR 309), February 15, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674127

OCCUPATIONAL EXPOSURE

Volume 80 Screening level occupational exposure assessments for R107894 (CL303268) as an anti-foulant in paint applied to underwater hulls, EXP Project No. 47101, EXP Report No. 02001, January 11, 2002, EXP Corporation, OPPTS Draft Guideline Series 875.

MRID 45674128

Please consider assigning priority review status to this action since it satisfies the criteria as a TBTO replacement for anti-fouling use; TBTO will no longer be allowed by the International Maritime Organization (IMO) after 2003. The USEPA Antimicrobial Division has identified TBTO anti-fouling replacement products as a priority for receiving a high level of EPA resources in 2002-03 work plan.

Please contact me directly on any matters relating to this registration application. I can be reached by phone at 609-730-2607.

Sincerely,

Bill Goodwine

William R. Goodwine
Director
Plant & Material Protection Division

Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com

JANSSEN PHARMACEUTICA INC.

June 10, 2002

Mr. Marshall Swindell
Product Manager Team 33
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

SUBJECT: ECONEA™ Technical (Janssen Code No. R107894)
Application for Registration
Resubmission of Rejected Studies

Dear Mr. Swindell:

As noted in EPA's May 20, 2002 Report of Analysis for Compliance with PR Notice 86-5, Janssen Pharmaceutica Inc. has corrected the rejected studies and their deficiencies.

The corrected studies enclosed are:

Volume 1 Preliminary Analysis and Certification of Ingredient Limits for the Technical Grade of AC 303268, Report No. APBR 1212, February 7, 2002. BASF, OPPTS Draft Guideline 830.1550, 830.1700 & 830.1750.

MRID _____

Volume 2 Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303268: OPPTS 830.1600, "Description of Materials Used to Produce Product" and OPPTS 830.1620, "Description of Product Process, Report No. P-363.01, January 22, 2001. BASF. OPPTS Draft Guideline 830.1600 & 830.1620.

MRID _____

1125 TRENTON HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000

Volume 39 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Satisfying Avian LD50 Data Requirements for Mallard Ducks and Bobwhite Quail for AC303,630 (R107894 and Metabolite CL 325,195), Guideline 71-1

MRID _____

Volume 65 CL 322,248 - Toxicity to Amphipods (*Hyalella azateca*) During a 10-Day Sediment Exposure, Report No. 13751.6112 (Janssen Rpt. No. AGR 342), October 11, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID _____

I can be reached by phone at 609-730-2607 if you have any questions.

Sincerely,

Bill Goodwine

William R. Goodwine
Director
Plant & Material Protection Division
Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Meeting Minutes (3/7/2001)

Sigma Coatings USA
P.O. Box816
1401 Destrehan Ave.
Harvey, LA 70059

Attn.: Mike Winter
and
Janssen Pharmaceutica
Attn.: W. Goodwine

Subject: Pre-application Meeting For New Active Ingredient: AF028, and
New Antifoulant Paint Product: Sigma Nexxium
Meeting Held March 7, 2001

On the date referred to above members of the Antimicrobials Division (AD) held a pre-application meeting with representatives from Sigma Coatings, Janssen Pharmaceutica, and BASF Corporation. The attendees of the meeting are listed below:

USEPA/Antimicrobials Division

Marshall Swindell, Carlton Kempter, Karen P. Hicks, Jonathan Chen, Norman Cook, Kathryn Montague, Najim Shamim, Doreen Aviado, Winston Dang, Karen Leavy, and Timothy McMahon.

Company Representatives:

Nys Jan (Janssen, Belgium), Bill Goodwin (Janssen, USA), Frederick Hess (BASF, USA), Jane E. Harris (BASF, USA), Dolores A. Chiarello (BASF, USA), Mike Winter (Sigma Coatings).

The following is a description of the discussions held and decisions made during the meeting:

Administrative

The new active ingredient AF028 (aka R107894) is intended for use in antifouling paint product. The active is a metabolite of an insecticide currently registered with EPA The registered insecticide is an inactive precursor which is metabolized to form the new active ingredient. AF028 is intended to control the growth of barnacles. BASF will be manufacturing the new ai, Janssen will register the technical grade active, and Sigma Coatings will register the end-use formula.

Sigma Coating's proposed end-use formula will also contain the active ingredient Sea Nine 211 from [redacted] to control the growth of algae.. The initial end-use application will be for use on commercial vessels, and gov., and Navy ships. Sigma may seek use on pleasure crafts at a later date. Janssen and Sigma expect to file for registration of the technical and end-use application by the fourth quarter of this calender year. The new active is currently being used in Italy, Greece, and Spain for antifoulant use (for the last year).

In preparation for the meeting the companies submitted a listing of all data they have generated in support of the new active ingredient. These studies should be submitted in support of the TGAI in addition to the missing studies indicated below.

Toxicology

The new active ingredient functions by uncoupling oxidative phosphorilation in the mitochondria of cells. The level of toxicity is directly proportional to the rate of conversion of the precursor/parent compound to the new active. The conversion rate varies between species and sex.

To support the insecticide registration, BASF has conducted a number of toxicity studies on the precursor/parent compound. The company has calculated that the toxicity of the parent compound comes from the amount of the new active which is formed from cellular metabolism. On this basis the company proposes to use the current toxicity data on file with the agency for the parent compound. They will submit a justification for such an approach and copies of the completed science reviews for their toxicity data. AD indicated that this information will be reviewed at the time the application submittal.

The companies have generated acute toxicity data on the parent compound, the new active ingredient, two of the metabolites of the new active, and the end-use paint formulation. A complete data set may not be available for each of the above. The Skin Irritation study is missing for each.

Chemistry and Environmental Fate

Data was conducted on the actual new active ingredient and has not been reviewed by the Registration Division. Janssen has a complete chemistry data set on the new active, and Sigma has chemistry on the end-use formulation.

BASF did not conduct a Bioaccumulation study as they considered it not required because the POW under environmental conditions (pH 8 and higher) is lower than 3. AD indicated that we will determine if this rationale is correct. AD prefers to have the study.

A Photolysis study was not conducted because of the calculated short half-life in water. AD indicated that we will discuss this issue in house, but that the company should submit a complete rationale for a waiver of the study.

AD indicated that a paint leaching study will be needed. The company agreed to conduct the study. Sigma indicated that they are currently developing paint leaching studies at Case Laboratories (NJ).

Fish and Wildlife

AD/RASSB has determined that the following studies are OUTSTANDING and must be submitted to support the registration of this antifoulant (parent compound):

72-3a Estuarine/marine organism acute toxicity testing--fish
72-3b Estuarine/marine organism acute toxicity testing--oyster
72-3c Estuarine/marine organism acute toxicity testing--mysid
123-1 Terrestrial Plant Tier II Seedling Emergence test--rice (*Oryza sativa*) only
123-2 Aquatic Plant Tier II Testing--2 outstanding species (1 diatom and 1 blue-green alga)

The company has also agreed to submit a rationale for ecological effects toxicity testing with one or more of the degradates of this chemical . Additional data may be required pending review of this rationale.

Additionally, any data listed in the chart (provided with original meeting material) that the company has already generated or agreed to generate should be submitted.

Human Exposure

The companies were informed that they must submit application and post-application exposure information as follows:

Technical Bulletin
Product use information (TGAI & End use products)
Description of Human Activities

Application and post-application exposure test guidelines can refer to:
www.epa.gov/docs/OPPTS_Harmonize...ential_Exposure_Test_Giidelines/Series

pg 5

If the company intends to conduct an exposure study they should submit a testing protocol first, and consider the following areas of worker exposure for evaluation: manufacturing of the paint, application of paint, and post-application of paint. AD discussed possible submission of a "human health exposure risk assessment" in lieu of conducting a dermal/inhalation exposure monitoring study once the Agency has reviewed the toxicity data and established toxicological endpoint.

SUBMISSION BAR CODE # D820066 REVIEWER KM

S#F41978

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 43813-ET PM 33 ACTION CODE 115

DESCRIPTOR _____

[ ] CHILD RESISTANT PACKAGING: [ ] CERTIFICATION
[ ] NON-RESIDENTIAL USE ONLY
[ ] NOT APPLICABLE

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL

PROPOSED CLASSIFICATION: [ ] GENERAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
06 02 03	06 04 03	06 04 03

METHOD OF SUPPORT:
[ ] CITE ALL
[ ] SELECTIVE
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

FORMULATORS EXEMPTION
[ ] SUBMITTED
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
EFFICACY				
TOXICOLOGY				
HED TOX.				
ENVIRON. FATE				
FISH/WILDLIFE				
OTHER _____				

STATUS _____

RESPONSE CODE 38 RESPONSE DATE 4/29/04

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

APR 29 2004

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. William Goodwine
Senior Director of the Plant & Material Protection Division for,
Janssen Pharmaceutica, Inc.
1125 Trenton-Harbourton Road
Titusville, NJ 008560

Subject: ECONEA TM Technical
EPA File Symbol 43813-ET
Your Application Dated June 2nd, 2003
EPA Received Date June 4th, 2003

The application referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act(FIFRA), as amended, is incomplete.

Upon conducting a review of the submitted studies, the following comments apply:

Adsorption/Desorption of the Hydrolysis Products Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for an adsorption/desorption study in sediments.

Adsorption/Desorption Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for adsorption/desorption study in sediment.

Anaerobic Degradation Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for anaerobic degradation study in two water-sediment systems.

Hydrolysis Data for ECONEA:

This Hydrolysis study satisfies the data requirements and the findings/conclusions are scientifically sound.

Aerobic Degradation Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for aerobic bio-transformation study in two water-sediment systems.

Thank you for your submission of revised product labeling. It will be used during review of your application.

The product mentioned above has not passed the chemical screen; however, based upon our agreement to initiate a review of all submitted data, except toxicity data due to missing studies, data reviews are still being processed.

As per our letter of March 8th, 2003, due to the unusual circumstances associated with this new active ingredient, the Agency is still reviewing the ecological effects data and end-use application into review in the absence of a complete data package. Normally, a new active ingredient submission must be complete package before the Agency will start its review process.

Please note that when toxicology data are submitted they will be placed into review on a track independent of the environmental and other reviews.

The product may not be lawfully distributed in interstate commerce until the above discrepancies have been clarified.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely yours,

Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

APR 29 2004

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. William Goodwine
Senior Director of the Plant & Material Protection Division for,
Janssen Pharmaceutica, Inc.
1125 Trenton-Harbourton Road
Titusville, NJ 008560

Subject: ECONEA TM Technical
EPA File Symbol 43813-ET
Your Application Dated June 2nd, 2003
EPA Received Date June 4th, 2003

The application referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act(FIFRA), as amended, is incomplete.

Upon conducting a review of the submitted studies, the following comments apply:

Adsorption/Desorption of the Hydrolysis Products Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for an adsorption/desorption study in sediments.

Adsorption/Desorption Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for adsorption/desorption study in sediment.

Anaerobic Degradation Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for anaerobic degradation study in two water-sediment systems.

Hydrolysis Data for ECONEA:

This Hydrolysis study satisfies the data requirements and the findings/conclusions are scientifically sound.

Aerobic Degradation Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for aerobic bio-transformation study in two water-sediment systems.

Thank you for your submission of revised product labeling. It will be used during review of your application.

The product mentioned above has not passed the chemical screen; however, based upon our agreement to initiate a review of all submitted data, except toxicity data due to missing studies, data reviews are still being processed.

As per our letter of March 8th, 2003, due to the unusual circumstances associated with this new active ingredient, the Agency is still reviewing the ecological effects data and end-use application into review in the absence of a complete data package. Normally, a new active ingredient submission must be complete package before the Agency will start its review process.

Please note that when toxicology data are submitted they will be placed into review on a track independent of the environmental and other reviews.

The product may not be lawfully distributed in interstate commerce until the above discrepancies have been clarified.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely yours,

Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)

EPA
United States
Environmental Protection
Agency

Date: 4/19/04

SUBJECT: Econea Ecotoxicity Studies Submitted in Support of Antifoulant Paint Use

DP Barcodes: 289026, 290345, 292015
PC Code: 119093

FROM: Richard C. Petrie, Team 3 Leader, Agronomist R.C. Petrie 4/19/04
Kathryn Montague, Biologist Kathryn Y Montague 4/19/04
OPP/AD/RASSB
Antimicrobial Division (7501C)

THRU : Norm Cook. Norman P. Cook 4/23/04
Chief, RASSB
Antimicrobial Division (7501C)

TO: Marshall Swindell, RM 33
Antimicrobial Division (7501C)

The RASSB has reviewed ecotoxicity studies submitted in support of chlorfenapyr (Econea) registration as an antifoulant paint. Numerous aquatic animal, plant and whole sediment toxicity tests were submitted for the active ingredient R107894, the first primary degradate CL 322,250, and two additional degradates CL322,248 and CL 325,195. A total of 67 studies were reviewed. See the "Status/Results of Submitted Econea Ecological Effects Studies - 4/13/04" below:

Status/Results of Submitted Econea Ecological Effects Studies

Econea Technical (R107894, AC303,268)

Study	Species	MRID	Status	Results
Avian acute oral	bobwhite	434928-09	Core	LD50 = 24.7, NOEL = 6 mg/kg
Avian acute oral	mallard	434928-08	Core	LD50 = 77, NOEL = 20 mg/kg
FW fish acute	bluegill	456740-02	Invalid	
FW fish acute	trout	456740-01	Invalid	
FW invert acute	daphnid	456740-04 457069-01	Invalid Invalid	
FW fish ELS	zebra fish	458939-01	Core	NOEC = 0.17 MATC = 0.25 ug/L
FW invert life cycle	daphnid	456740-08	Invalid	
ME fish acute	sheepshead	456740-03	Supplemental	LD50 = 23.71, NOEC = 10 ug/L
ME mollusk acute	E. oyster	456740-05	Supplemental	EC50 = 0.62, NOEC , 0.19 ug/L
ME invert acute	mysid	456740-06	Core	LD50 = 0.94 ug/L
ME fish ELS	Sheepshead	456740-07	Core	NOEC = 4.3, LOEC = 8.7 ug/L
ME invert lifecycle	mysid	456740-09	Supplemental	NOEC = 0.25, MATC = 0.36 ug/L
Whole sediment, FW	*Hyalella*	456740-10	Core	LC50 = 2.2, NOEC = 1.0 mg ai/L
Whole sediment, ME	*Leptocheirus*	456740-11	Core	LC50= 1.1, NOEC = 0.50 mg ai/L
Green alga	*Selenastrum*	456741-17	Supplemental	EC40 = 4.49, NOEC = 3.1 ug/L
Blue-green cyanobacteria	*Anabaena*	458939-02	Core	EC50 = 350, NOEC = 9.2 ug/L
FW diatom	*Navicula*	458939-03	Core	EC50 = 5.5, NOEC=0.99 ug/L
ME diatom	*Skeletonema*	456741-18	Supplemental	EC50 = 2.88, NOEC=0.54 ug/L
Seedling emergence	Rice	456741-15	Core	<25% inhib at 170 ug/L
Duckweed	*Lemna g.*	456741-16	Core	EC50 = 87.2, NOEC = 22.0 ug ai/L

Major Degradate, CL 322,250

Study	Species	MRID	Status	Results
FW fish acute	bluegill	456740-23	Invalid	
FW fish acute	trout	456740-22	Invalid	
FW invert acute	daphnid	456741-02 457069-03	Supplemental Supplemental	LD50 = 0.65, NOEC <0.43 mg/L LD50 = 1.57 mg/L
FW fish ELS	zebra fish	456741-05	Invalid	
FW invert life cycle	daphnid	456741-07	Invalid	
ME fish acute	sheepshead	456741-01	Supplemental	LD50 >0.95, NOEC = 0.95 mg/L
ME mollusk acute	E. oyster	456741-03	Core	EC50=0.31, NOEC=0.046 mg/L
ME invert acute	mysid	456741-04	Core	LD50 = 0.57, NOEC , 0.41 mg/L
ME fish ELS	Sheepshead	456741-06	Core	NOEC = 0.24, MATC = 0.35 ug/L
Whole sediment, FW	*Hyalella*	456741-08	Core	LC50 = >35.0, NOEC = >35.0 mg ai/L
Whole sediment, ME	*Leptochairus*	456741-09	Core	LC50 = >70.0, NOEC = >70.0 mg ai/L
Green alga	*Selenastrum*	456741-23	Supplemental	EC40 > 4.54, NOEC = 1.15 mg/L
Blue-green cyanobacteria	*Anabeana*	458939-07	Supplemental	EC50 > 0.83, NOEC = 0.83 mg/L
FW diatom	*Navicula*	458939-08	Supplemental	EC50 > 0.93, NOEC=0.93 mg/L
ME diatom	*Skeletonema*	456741-24	Supplemental	EC50 = 1.14, EC05 = 0.18 mg/L
Duckweed	*Lemna g.*	456741-22	Supplemental	EC50 = >0.99, NOEC = 0.53 mg ai/L

Minor Degradate, CL325, 195

Study	Species	MRID	Status	Results
Avian acute oral	bobwhite	444526-11	Core	LD50 = 741, NOEC = 192 mg/kg
Avian acute oral	Mallard	444526-12	Core	LD50 > 2250, NOEC = 2250 mg/kg
FW fish acute	bluegill	444526-17	Invalid	
FW fish acute	trout	456740-01	Invalid	
FW invert acute	daphnid	444526-18 457069-02	Invalid Supplemental	LD50 = 3.57 ug/L
FW fish ELS	zebra fish	456740-16	Invalid	
FW invert life cycle	daphnid	456740-18	Invalid	
ME fish acute	sheepshead	456740-13	Supplemental	LD50 >16, NOEC = 16 mg/L
ME mollusk acute	E. oyster	456740-14	Core	EC50>14, NOEC=6.9 mg/L
ME invert acute	mysid	456740-15	Core	LD50 = 12.0, NOEC = 10.0 mg/L
ME fish ELS	Sheepshead	456740-17	Core	NOEC = 1.3 MATC = 1.9 mg/L
Whole sediment, FW	*Hyalella*	456740-19	Supplemental	LC50 = >49.0, NOEC = 49.0 mg ai/L
Whole sediment, ME	*Leptocheirus*	456740-20	Core	LC50 = >27.0, NOEC = >27.0 mg ai/L
Green alga	*Selenastrum*	456741-20	Supplemental	EC50=0.44, EC05 = 0.23 mg/L
Blue-green cyanobacteria	*Anabaena*	459452-01	Core	EC50= 6.5, NOEC = 1.40 mg/L
FW diatom	*Navicula*	458939-06	Core	EC50= 1.51, NOEC=0.85 mg/L
ME diatom	*Skeletonema*	456741-21	Supplemental	EC50 = 0.47, NOEC<0.28 mg/L
Duckweed	*Lemna g.*	456741-19	Core	EC50 = 13.0, NOEC = 5.9 mg ai/L

Additional Degradate, CL 322,248 (not found in fate studies)

Study	Species	MRID	Status	Results
FW fish acute	bluegill	456741-11	Invalid	
FW fish acute	trout	456741-10	Invalid	
FW invert acute	daphnid	456741-12	Supplemental	LD50 = 16.8 mg/L
FW invert life cycle	daphnid	456741-13	Supplemental	NOEC, 1.37, MATC = 3.85 mg/L
Whole sediment, FW	*Hyalella*	456958-04	Supplemental	LC50 = >49.0, NOEC = 49.0 mg ai/L
Whole sediment, ME	*Leptocheirus*	456741-14	Core	LC50 = >75.0, NOEC = >75.0 mg ai/L
Green alga	*Selenastrum*	456741-26	Supplemental	EC40 > 1.99, NOEC = 1.99 mg/L
Blue-green cyanobacteria	*Anabeana*	458939-04	Supplemental	EC50 > 1.0, NOEC = 1.0 mg/L
FW diatom	*Navicula*	458939-05	Supplemental	EC50 > 0.98, NOEC=0.98 mg/L
ME diatom	*Skeletonema*	456741-27	Supplemental	EC50 = 1.20, NOEC=0.16 mg/L
Duckweed	*Lemna g.*	456741-25	Supplemental	EC50 = >0.93, NOEC = 0.93 mg ai/L

The following table lists outstanding ecotoxicology studies. RASSB had determined that due to rapid degradation of R107894 to CL322,250 many of the acute and chronic toxicity tests must be repeated (invalid or supplemental ratings). Fish and oyster BCF's are also required for these two chemicals. The CL322-248 degradate, which is the debrominated form of CL322,250 found under anaerobic conditions and in saltwater, is a toxicity concern as well.

Further, bromine released during the degradation process must be characterized by the registrant. A significant amount of bromine could be toxic to aquatic plants and animals and may necessitate ecotoxicity testing for risk assessment.

Econea - Outstanding Eco Effects Data

Econea Technical (aka R107894, AC303,268)

Study	Species	Status
Avian dietary - 850.2200	bobwhite	Reserved 43498-09 ccc
Avian dietary - 850.2200	mallard	Required
FW fish acute - 850.1075 ✓	bluegill	Required 44452677 bid unacceptable
FW fish acute - 850.1075 ✓	trout	Required 45674020-01 invalid
FW invert acute - 850.1010 ✓	daphnid	Required 45670690-02 supplemental
FW invert life cycle - 850.1300 ✓	daphnid	Required 45670690-18 invalid
Fish BCF - 850.1730	bluegill	Required
Oyster BCF - 850.1710	E. oyster	Required
Green Algae - 850.5400	*Selenastrum capricornutum*	Required
Marine diatom - 850.5400	*Skeletonema costatum*	Required 45687418

Major Degradate, CL 322,250

Study	Species	Status
Avian acute oral - 850.2100	mallard	Required
Avian dietary - 850.2200	bobwhite	Reserved
Avian dietary - 850.2200	mallard	Required
FW fish acute - 850.1075 ✓✓	bluegill	Required 45674022 45674023
FW fish acute - 850.1075 ✓ ✓	trout	Required 45674023
FW invert acute - 850.1010 ✓	daphnid	Required 45687405 invalid
FW fish ELS - 850.1400 ✓	zebra fish	Required
FW invert life cycle - 850.1300 ✓	daphnid	Required 45687404 invalid
ME fish acute - 850.1075 ✓	sheepshead	Required 45687401 supplemental
ME invert lifecycle - 850.1350	mysid	Required
Fish BCF - 850.1730	bluegill	Required
Oyster BCF - 850.1710	E. oyster	Required
Marine diatom - 850.5400 ✓	*Skeletonema costatum*	Required 45687424 supplemental

Degradate, CL 322,248 (de-brominated CL322,250 - found in saltwater and anaerobic conditions)

Study	Species	MRID
Avian acute oral - 850.2100	mallard	Required
Avian dietary - 850.2200	bobwhite	Required
Avian dietary - 850.2200	mallard	Required
ME fish acute - 850.1075	sheepshead	Required
ME mollusk acute - 850.1025	E. oyster	Required
ME invert acute - 850.1035	mysid	Required
ME fish ELS - 850.1075	Sheepshead	Required
ME invert lifecycle - 850.1350 ✓	mysid	Required 45674/-04 core

See current OPP policy regarding use of dechlorinated water in freshwater aquatic toxicity tests below.

U. S. ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM **DATE:** September 10 , 1999

SUBJECT: Use of dechlorinated water in freshwater aquatic toxicity tests

FROM: The Aquatic Technical Team
Environmental Fate and Effects Division

THROUGH: Aquatic Technical Team Co-chairs
Thomas M. Steeger, Fishery Biologist
Brian Montague, Fishery Biologist

TO: Mary Frankenberry, Chairperson
Science Policy Panel
Environmental Fate and Effects Division

The Aquatic Biology Technical Team (ABTT) has reviewed the issues regarding the use of dechlorinated water in freshwater aquatic toxicity tests and believes that it is necessary to recommend a consistent policy in EFED regarding studies that use dechlorinated water. Currently there is inconsistency in the classification of aquatic toxicity tests where dechlorinated water has been used; e.g., some scientists reject the study, wheres others accept the study with admonishment against its use in testing. The purpose of this memo is to clarify EFED policy on the use of dechlorinated water in aquatic laboratory testing, both acute and chronic and thereby establish consistency among scientists in the handling of studies where dechlorinated water is used. Regardless of whether the test species is fish, macroinvertebrates or amphibians, if dechlorinated water is used in aquatic toxicity tests, it must be shown that first instar daphnids can survive unencumbered in the test water for 48 hours without food; otherwise, residual chlorine must be measured to demonstrate that it falls below specific levels. If a study fails to comply with these criteria, it should be classified as invalid since the effects of residual chlorine could not be dismissed.

It is generally recognized that chlorine-produced oxidants are toxic to aquatic animals. Chlorinated water should not be used in aquatic testing because the process of dechlorination is often incomplete. **EPA's 1994 Reregistration Rejection Rate Analysis** states the Agency strongly recommends against the use of dechlorinated water, and that if its use cannot be avoided then the biological responses for the control organisms **and** chemical analyses must meet acceptable criteria (undefined in document). **ASTM E 729 -88a** (Standard Guide for Conducting Acute Toxicity Tests With Fishes, Macroinvertebrates, and Amphibians; 1989) states that if dechlorinated water is used, either *(a)* it must be shown that a sensitive aquatic species will survive, grow, and reproduce acceptably in it, **or** *(b)* it must be shown at least three times each week on nonconsecutive days that in fresh samples of dilution water either *(1) Acartia tonsa*, mysids (less than 24-h post release from the brood sac), bivalve mollusc larvae, or daphnids (less than 24-h old) do not show more signs of stress, such as discoloration, unusual behavior, or death, when held in water for at least 48 h without food than when similarly held in water that was not chlorinated and dechlorinated, **or** *(2)* the concentration of residual chlorine in fresh water is less than 11 ug/l or the concentration of chlorine-produced oxidants in salt water is less than 7.5 ug/l. **EPA's 1975 publication** (EPA-660/3-75-009; Methods for Acute Toxicity Tests With Fish, Macroinvertebrates, and Amphibians) states "If a dechlorinated water is used, at the beginning of STATIC tests and daily during FLOW-THROUGH tests either it must be shown that first instar daphnids can survive in it for 48 hours without food or residual chlorine must be measured."

It is clear from the preceding discussion that either residual chlorine levels must be documented or toxicity tests on daphnids must be conducted to establish that chlorine residues had no effect. Failure to comply with these testing requirements if dechlorinated water is in use, would confound efforts to distinguish between what may be treatment effects and effects due to residual chlorine. In cases where dechlorinated water was used and the recommended tests regarding the effects of residual chlorine were <u>not</u> performed, the Aquatic Biology Technical Team recommends that the study be classified as invalid.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 22, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Review of Adsorption/Desorption of the Hydrolysis Products Study for ECONEA™ Technical Containing AC 303268 Antifoulant

TO: Marshall Swindell, Product Manager, Team 33
Regulatory Management Branch I
Antimicrobials Division (7510C)

FROM: Srinivas Gowda, Microbiologist/Chemist Srinivas Gowda 1/22/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

THRU: Siroos Mostaghimi, Acting Team Leader, Team One 1/28/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

Norm Cook, Chief 1/28/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

DP Barcodes: D289027
Decision #: 220066
Case Type: New Registration
PC Codes: 119093
Chemical Name: 1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

EPA File Symbol: 43813-ET
MRID No.: 456739-14
Data Submitter: Janssen Pharmaceutica Inc.
CAS#: 122454-29-9
Common Name: AC303268

INTRODUCTION:

Janssen Pharmaceutica Inc. has submitted the adsorption/desorption of hydrolysis products of the active ingredient, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- (also known as AC 303268) study to meet the U.S. Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide Assessment Guidelines, Subdivision N, § 163-1 in support of new registration of ECONEA™ Technical, EPA File Symbol 43813-ET, for formulation of antifouling treatment products. The submitted adsorption/desorption of the hydrolysis products of AC303268 (in sediment) study has undergone review by Srinivas Gowda of Antimicrobials Division's Risk Assessment and Science Support Branch.

BACKGROUND:

1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- is a new active ingredient in ECONEA™ Technical Anti-fouling Preservative. It is also known as AC303268.

CONCLUSIONS:

1a. The adsorption Freundlich constants were K_f=189 in sandy loam, K_f=357 in silt loam, K_f=14 in sand, and K_f=119 in loam sediments.

1b. The adsorption coefficient K_a values ranged from 132 to 179 in sandy loam, 266 to 383 in silt loam, 7 to 10 in sand, and 97 to 114 in loam sediments. The adsorption K_{oc} values ranged from 6000 to 8136 in sandy loam, 13275 to 19150 in silt loam, 1000 to 1429 in sand, and 2772 to 3257 in loam sediments.

2a. The desorption coefficient K_d values ranged from 152 to 266 in sandy loam, 379 to 635 in silt loam, 11 to 16 in sand, and 136 to 174 in loam sediments. The desorption K_{oc} values ranged from 6887 to 12091 in sandy loam, 18950 to 31725 in silt loam, 1571 to 2286 in sand, and 3886 to 4972 in loam sediments. The desorption K_d and K_{oc} values were higher than those obtained for adsorption.

RECOMMENDATIONS:

This study is classified as acceptable and satisfies the guideline requirement for an adsorption/desorption study in sediments. RASSB recommends that the Adsorption/Desorption (of the Hydrolysis Products of AC 303268 in fresh and marine water sediments) studies be accepted in support of ECONEA™ Technical MUP registration.

ADSORPTION/DESORPTION OF THE HYDROLYSIS PRODUCTS

DATA EVALUATION REPORT

PRODUCT FORMULATION: ECONEA™ Technical Anti-Fouling Preservative

ACTIVE INGREDIENT: 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl), also known as AC 303268

BACKGROUND: The study was submitted to evaluate the adsorption/desorption of the hydrolysis products of the active ingredient AC 303268 in sediments. The study was conducted according to the Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide Assessment Guidelines, Subdivision N, § 163-1.

CITATION:
Mackie, J.A. 1999. Adsorption/Desorption of the Hydrolysis Products of [^{14}C]-R-107894 in Sediments. Inveresk Research, Tranent, EH33 2NE, Scotland. Inveresk Report No. 16693. Inveresk Project No. 390770. Sponsor: Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse, Belgium. January 22, 1999.

EXECUTIVE SUMMARY:

The adsorption/desorption characteristics of the hydrolysis product of [^{14}C]-R107894 (i.e., [^{14}C]-CL 322,250) were studied in a sandy loam fresh water sediment (pH 6.5, 2.2% organic carbon) and a silt loam fresh water sediment (pH 4.2, 2.0% organic carbon) both from the Scottish Agricultural College in Auchincruive, Scotland; and a sand marine sediment (pH 7.1, 0.7% organic carbon) and a loam marine sediment (pH 7.7, 3.5% organic carbon) from Orkney Water Test Centre in Orkney, Scotland and University Marine Biological Station Millport, Isle of Cumbrae, Scotland, respectively, in batch equilibrium experiments. The experiment was conducted in accordance with the OECD Guidelines for the Testing of Chemicals, Document 106 (1980), EC Directive 91/414, EPA Pesticide Assessment Guidelines, Subdivision N, Paragraph 163-1 and the OPPTS 835.1220 Guidelines (January 1998), and in compliance with the GLP requirements as specified in 40 CFR Part 160.

The adsorption phase of the study was carried out by equilibrating oven-dried fresh water sediments with [^{14}C]-CL 322,250 at 0.433, 0.248, 0.100, and 0.051 µg/g (expressed as R107894 equivalents) and oven-dried marine sediments with [^{14}C]-CL 322,250 at 0.451, 0.249, 0.090, and 0.050 µg/g (expressed as R107894 equivalents) in the dark at 20°C for 16 hours. The equilibrating solution used for the fresh water sediments was 0.01M $CaCl_2$ and seawater for the marine sediments, with a soil/sediment ratio of 2 grams sediment:10 grams solution. The desorption phase of the study was carried out by adding a weight of 0.01M calcium chloride or seawater, approximately equal to that removed as supernatant during the adsorption phase of the study, to duplicate tubes for each sediment type. The tubes were shaken in the dark at 20°C for 16 hours.

The supernatant solution after adsorption and desorption was separated by centrifugation. Duplicate aliquots of the supernatant were analyzed by LSC. Each sediment pellet was extracted with acetonitrile for 1 hour, the extracts were separated by centrifugation, and duplicate aliquots were analyzed by LSC. For each individual sediment, an aliquot of the extract was concentrated under nitrogen and characterized and quantified by HPLC (Hewlett-Packard 1050 series equipped with a UV detector set at 280 nm) and TLC (Molecular Dynamics Phosphor Imager). The ^{14}C in the sediment residue after the adsorption and desorption steps was determined by combustion (Packard Sample Oxidiser, Model 306). The combusted products were absorbed in Carbo-Sorb®, mixed with Permafluor®E$^+$ and the radioactivity was determined by LSC. The

adsorption parameters were calculated using the Freundlich adsorption isotherm.

The stability of the test material in the presence of sediment, following equilibration, was investigated by HPLC. Under the conditions of the test, [^{14}C]-CL 322,250 was shown to be stable. The mass balance at the end of adsorption phase of the study was 97.8, 91.8, 93.3, and 93.3 percent of the applied radioactivity in sandy loam, silt loam, sand, and loam sediments, respectively. The mass balance at the end of desorption phase was 99.9, 93.8, 96.3, and 98.7 percent of the applied radioactivity in sandy loam, silt loam, sand, and loam sediments, respectively.

After 16 hours of equilibration, 96.4, 96.5, 97.0, and 97.3 percent of the applied radioactivity (expressed as R107894 equivalents) was adsorbed in sandy loam sediment at initial concentrations of 433, 248, 100, and 51 ng equiv/g, respectively. After 16 hours of equilibration, 98.2, 98.3, 98.6, and 98.7 percent of the applied radioactivity was adsorbed in silt loam sediment at initial concentrations of 433, 248, 100, and 51 ng equiv/g, respectively. After 16 hours of equilibration, 58.1, 60.2, 61.2, and 67.1 percent of the applied radioactivity was adsorbed in sand sediment at initial concentrations of 451, 249, 90, and 50 ng equiv/g, respectively. After 16 hours of equilibration, 95.1, 95.4, 95.4, and 95.8 percent of the applied radioactivity was adsorbed in loam sediment at initial concentrations of 451, 249, 90, and 50 ng equiv/g, respectively. The adsorption Freundlich constants were K_f = 189 (1/n = 0.864) in sandy loam, K_f = 357 (1/n = 0.859) in silt loam, K_f = 14 (1/n = 0.857) in sand, and K_f = 119 (1/n = 0.935) in loam sediments.

The adsorption coefficient K_a values ranged from 132 to 179 in sandy loam, 266 to 383 in silt loam, 7 to 10 in sand, and 97 to 114 in loam sediments. The adsorption K_{oc} values ranged from 6000 to 8136 in sandy loam, 13275 to 19150 in silt loam, 1000 to 1429 in sand, and 2772 to 3257 in loam sediments.

After 16 hours of equilibration, 3.15, 2.68, 2.00, and 1.82 percent of the adsorbed radioactivity was desorbed in sandy loam sediment at initial concentrations of 433, 248, 100, and 51 ng equiv/g, respectively. After 16 hours of equilibration, 1.30, 1.18, 0.85, 0.78 percent of the adsorbed radioactivity was desorbed in silt loam sediment at initial concentrations of 433, 248, 100, and 51 ng equiv/g, respectively. After 16 hours of equilibration, 18.5, 18.4, 18.9, and 16.1 percent of the adsorbed radioactivity was desorbed in sand sediment at initial concentrations of 451, 249, 90, and 50 ng equiv/g, respectively. After 16 hours of equilibration, 3.50, 3.30, 3.22, and 2.76 percent of the adsorbed radioactivity was desorbed in loam sediment at initial concentrations of 451, 249, 90, and 50 ng equiv/g, respectively.

The desorption coefficient K_d values ranged from 152 to 266 in sandy loam, 379 to 635 in silt loam, 11 to 16 in sand, and 136 to 174 in loam sediments. The desorption K_{oc} values ranged from 6887 to 12091 in sandy loam, 18950 to 31725 in silt loam, 1571 to 2286 in sand, and 3886 to 4972 in loam sediments. The desorption K_d and K_{oc} values were higher than those obtained for adsorption.

Results Synopsis:

Sediment type:	Sandy Loam
Amount adsorbed:	96.4 to 97.3% as percentage of the applied
Adsorption K_a:	132 to 179
Adsorption K_{oc}:	6000 to 8136
Amount desorbed:	1.82 to 3.15% as percentage of the adsorbed
Desorption K_d:	156 to 266
Desorption K_{oc}:	6887 to 12091

Sediment type:	Silt Loam
Amount adsorbed:	98.2 to 98.7% as percentage of the applied
Adsorption K_a:	266 to 383
Adsorption K_{oc}:	13275 to 19150
Amount desorbed:	0.78 to 1.30% as percentage of the adsorbed
Desorption K_d:	379 to 635
Desorption K_{oc}:	18950 to 31725

Sediment type:	Sand
Amount adsorbed:	58.1 to 67.1% as percentage of the applied
Adsorption K_a:	7 to 10
Adsorption K_{oc}:	1000 to 1429
Amount desorbed:	16.1 to 18.9% as percentage of the adsorbed
Desorption K_d:	11 to 16
Desorption K_{oc}:	1571 to 2286

Sediment type:	Loam
Amount adsorbed:	95.1 to 95.8% as percentage of the applied
Adsorption K_a:	97 to 114
Adsorption K_{oc}:	2772 to 3257
Amount desorbed:	2.76 to 3.50% as percentage of the adsorbed
Desorption K_d:	136 to 174
Desorption K_{oc}:	3886 to 4972

Study Acceptability: This study is classified acceptable and satisfies the guideline requirements for an adsorption/desorption study in sediments.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The study was conducted in accordance with the OECD Guidelines for the Testing of Chemicals, Document 106 (1980), EC Directive 91/414, EPA Pesticide Assessment Guidelines, Subdivision N, Paragraph 163-1 and the OPPTS 835,1220 Guideline (January 1998).

The Deviations from guidelines included: 1) no control solutions were tested in the study; 2) complete sediment properties and storage conditions were not reported; and 3) the three sediments selected were slightly different than those recommended by the guidelines. These deviations from the guidelines do not appear to affect the validity of the study.

COMPLIANCE: The work was performed in accordance with the GLP requirements as specified in 40 CFR Part 160. A signed and dated GLP Compliance Statement, Quality Assurance Statement, and Statement of No Data Confidentiality Claims were provided.

A. MATERIALS:

1. Test Material [Phenyl-^{14}C(U)]-R107894

Chemical Structure: Refer to Attachment I for structures of R107894 with position of carbon-14 label.

Description: [Phenyl-^{14}C(U)]-R107894, also known as CL 303,268 supplied by American Cyanamid, Princeton, USA. The test material was supplied in ethanol at a concentration of ca 11 mg/ml.

Purity:	Lot/Batch No.:	101-077-026
	Analytical purity:	>99%
	Radiochemical purity:	>99%
	Specific activity:	26.4 mCi/mmol, 75.4 μCi/mg
	Locations of the label:	

Storage conditions of test chemicals: Not stated.

Physio-chemical properties of [^{14}C]-R107894:

Parameter	Values	Comments
Water solubility	NR	
Vapor pressure	NR	
UV absorption	NR	
pK_a	NR	
K_{ow}	NR	
Stability of Compound at room temperature		The exact rate of decomposition is unknown. However, it can be assumed that the product may decompose at a rate of approximately 0.5% per month when stored at -20°C under argon.

2. Sediment Characteristics

Table 1: Description of sediment collection and storage.

	Fresh Water Sediments		Marine Sediments	
Description (USDA Classification)	**Sandy Loam (Inveresk Code S 242)**	**Silt Loam (Inveresk Code S 243)**	**Sand (Inveresk Code S 241)**	**Loam (Inveresk Code S 244)**
Geographic location	Scottish Agricultural College, Auchincruive, Scotland	Scottish Agricultural College, Auchincruive, Scotland	Orkney Water Test Centre, Orkney, Scotland	University Marine Biological Station Millport, Isle of Cumbrae, Scotland
Pesticide use history at the collection site	NR	NR	NR	NR
Collection procedures	NR	NR	NR	NR
Sampling depth (cm)	NR	NR	NR	NR
Storage conditions	NR	NR	NR	NR
Storage length	NR	NR	NR	NR
Sediment preparation	Sieved (2 mm), centrifuged (1000 rpm, 15 mins)	Sieved (2 mm), centrifuged (1000 rpm, 15 mins)	Sieved (2 mm), centrifuged (1000 rpm, 15 mins)	Sieved (2 mm), centrifuged (1000 rpm, 15 mins)

Table 2: Properties of the sediments.

	Fresh Water Sediments		Marine Sediments	
Property	Sandy Loam (Inveresk Code S 242)	Silt Loam (Inveresk Code S 243)	Sand (Inveresk Code S 241)	Loam (Inveresk Code S 244)
Sediment Texture				
% sand	66.8	20.39	90.04	27.86
% silt	19.71	59.93	7.55	46.47
% clay	13.49	19.68	2.41	25.67
pH	6.5	4.2	7.1	7.7
Organic carbon (%)	2.2	2	0.7	3.5
CEC (meq/100 g)	16.9	18.8	5.2	15.7
Moisture at 1/3 atm (%)	2.5	1.6	0.8	2.1
Bulk density (g/cm^3)	NR	NR	NR	NR
Biomass (mg microbial C/100 g or CFU or other)	NR	NR	NR	NR
Sediment taxonomic classification	NR	NR	NR	NR
Sol mapping unit (for EPA)	NR	NR	NR	NR

C. STUDY DESIGN:

1. Preliminary study:

Adsorption of [^{14}C]-CL 322,250 to Glass:

Solutions of [^{14}C]-CL 322,250 in 0.01 M calcium chloride and seawater were prepared at a nominal concentration of 0.5 µg/g R107894 equivalents (as determined by LSC). Duplicate aliquots of each solution were transferred to screw-capped glass centrifuge tubes. The tubes were shaken on an end-over-end shaker for 16 hours in the dark at 20 ± 2°C. Following shaking, duplicate aliquots from each tube were submitted for LSC. No radioactivity was lost from solution contained in the centrifuge tubes, which showed that the test material did not adsorb to the glass apparatus.

Stability of [^{14}C]-CL 322,250:

The stability of [^{14}C]-CL 322,250 at 20 ± 2°C in 0.01 M calcium chloride and seawater following

24 and 48 hours was determined by HPLC. Under the test conditions, the hydrolysis products of [^{14}C]-R107894 were shown to be stable.

2. <u>Definitive study experimental conditions:</u>

Table 3: Study design for the adsorption phase.

		Fresh Water Sediments		Marine Sediments	
Parameters		**Sandy Loam (USDA classification) Code S 242**	**Silt Loam (USDA classification) Code S 243**	**Sand (USDA classification) Code S 241**	**Loam (USDA classification) Code S 244**
Condition of sediment		Oven-dried	Oven-dried	Oven-dried	Oven-dried
Have these sediments been used for other laboratory studies ?		NR	NR	NR	NR
Sediment (g/replicate)		2 grams	2 grams	2 grams	2 grams
Equilibrium solution used		0.01M calcium chloride	0.01M calcium chloride	Seawater	Seawater
Control used (with salt solution only)		No	No	No	No
Test material concentrations	Nominal application rates (µg equiv/g sediment)	0.05 to 0.5 µg equiv/g	0.05 to 0.5 µg equiv/g	0.05 to 0.5 µg equiv/g	0.05 to 0.5 µg equiv/g
	Analytically measured concentrations (µg equiv/g)	0.433 0.248 0.100 0.051	0.433 0.248 0.100 0.051	0.451 0.249 0.090 0.050	0.451 0.249 0.090 0.050
Identity and concentration of co-solvent, if any		Up to 0.1% acetonitrile	Up to 0.1% acetonitrile	Up to 0.1% acetonitrile	Up to 0.1% acetonitrile
Sediment:solution ratio (gram sediment:gram solution)		0.0902777778	0.0902777778	0.090277778	0.09027778
Initial pH of the equilibration solution, if provided					
No. of replications	Controls	0	0	0	0
	Treatments	2	2	2	2
Equilibration	Time	16 hours	16 hours	16 hours	16 hours
	Temperature (°C)	20 ± 2°C	20 ± 2°C	20 ± 2°C	20 ± 2°C
	Darkness	Yes	Yes	Yes	Yes

Parameters		Sandy Loam (USDA classification) Code S 242	Silt Loam (USDA classification) Code S 243	Sand (USDA classification) Code S 241	Loam (USDA classification) Code S 244
	Shaking method	Inversion	Inversion	Inversion	Inversion
	Shaking time	16 hours	16 hours	16 hours	16 hours
Method of separation of supernatant		Centrifugation	Centrifugation	Centrifugation	Centrifugation
Centrifugation	Speed (rpm)	2000	2000	2000	2000
	Duration (min)	10	10	10	10
	Method of separation of sediment and solution	Centrifugation	Centrifugation	Centrifugation	Centrifugation

Table 4: Study design for the desorption phase.

		Fresh Water Sediments		Marine Sediments	
Parameters		Sandy Loam (USDA classification) Code S 242	Silt Loam (USDA classification) Code S 243	Sand (USDA classification) Code S 241	Loam (USDA classification) Code S 244
Were the sediment residues from the adsorption phase used?		Yes	Yes	Yes	Yes
Amount of test material present in the adsorbed state/adsorbed amount (µg equiv/g)	concentration 1	2078	2118	1317	2145
	concentration 2	1197	1222	751	1185
	concentration 3	485	493	275	432
	concentration 4	249	253	168	240
No. of desorption cycles		1 (16 hours)	1 (16 hours)	1 (16 hours)	1 (16 hours)
Equilibration solution and quantity used per treatment for desorption		0.01 M $CaCl_2$	0.01 M $CaCl_2$	Seawater	Seawater
Sediment:solution ratio (gram sediment: gram solution)		0.09027778	0.09027778	0.09027778	0.09027778
Replications	Controls	0	0	0	0
	Treatments	2	2	2	2
Desorption equilibration	Time	16 hours	16 hours	16 hours	16 hours
	Temperature (°C)	20 ± 2°C	20 ± 2°C	20 ± 2°C	20 ± 2°C
	Darkness	Yes	Yes	Yes	Yes
	Shaking method	Inversion	Inversion	Inversion	Inversion
	Shaking time	16 hours	16 hours	16 hours	16 hours

Parameters		Fresh Water Sediments		Marine Sediments	
		Sandy Loam (USDA classification) Code S 242	Silt Loam (USDA classification) Code S 243	Sand (USDA classification) Code S 241	Loam (USDA classification) Code S 244
Centrifugation	Speed (rpm)	2000	2000	2000	2000
	Duration (min)	10 min	10 min	10 min	10 min
	Method of separation of sediment and solution	Centrifugation	Centrifugation	Centrifugation	Centrifugation

3. Description of analytical procedures:

Extraction/clean up/concentration methods:

Following adsorption and desorption, the supernatant solution was separated by centrifugation and the supernatant was removed. Duplicate aliquots of supernatant were analyzed by LSC. The remainder of each supernatant was then acidified to pH 3 using 2M HCl to prevent further hydrolysis of [^{14}C]-R107894.

Each sediment pellet was extracted with acetonitrile for 1 hour, the extracts were separated by centrifugation, and duplicate aliquots were analyzed by LSC. For each individual sediment, an aliquot of the extract was concentrated under nitrogen and characterized and quantified by HPLC and TLC. The HPLC analysis was carried out using a Hewlett-Packard 1050 series equipped with an autosampler, UV detector (280 nm), and a solvent programmer connected to an Intersil Phenyl guard and HPLC column (1 cm and 25 cm x 4.6 mm; 5 µm; Hichrom) and a Packard Flo-One A-100 Series radioactivity monitor. The following mobile phases and gradient were used at a flow rate of 1.0 mL/min: acetonitrile:0.01M sodium citrate buffer (pH 4) (5:95, 95:5, v:v). The recovered radioactivity of the eluate was quantified by LSC. Non-radiolabeled reference standards were dissolved in acetonitrile:water (6:4, v:v) and injected into the HPLC column individually and as a mixture to determine standard retention times. The reference standards were chromatographed with test solutions at regular intervals.

Aliquots of each sample were also analyzed by TLC using a silica gel 60_{F254} TLC plate developed in toluene:acetone:methanol:acetic acid (75:30:6:0.5, by volume). The solvent was allowed to develop to a height of 170 mm. Following chromatography, quantification of radioactivity present on TLC plates was performed using a Molecular Dynamics phosphor imager. Standards were visualized by irradiation with UV light (254 nm). Co-chromatography of standards with radioactivity was used for the tentative identification of degradation products. Non-radiolabeled R107894, CL 322,250 and CL 325,195 were chromatographed with each sample. The ^{14}C in the sediment residue after the adsorption and desorption steps was determined by combustion (Packard Sample Oxidiser, Model 306). The combusted products were absorbed in Carbo-Sorb®, mixed with Permafluor®E$^+$ and the radioactivity was determined by LSC.

The study author reported a limit of reliable determination of 30 dpm above background.

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS:

The stability of [^{14}C]-CL 322,250 in the presence of sand sediment was determined by analyzing adsorption supernatant samples at 24- and 48-hour equilibrium times. The results indicated that [^{14}C]-CL 322,250 was stable under the conditions of the test in the sand sediment. It was assumed that the test materials would also be stable in the remaining sediments.

Overall, the experimental conditions outlined in the study protocol were maintained throughout the study. The reported deviation from the protocol was listed as follows:

- The equilibrium phase adsorption supernatant samples from the sandy loam, silt loam, and loam; and isotherm test adsorption and desorption supernatant samples from sandy loam, silt loam and loam contained insufficient levels of radioactivity to permit chromatographic analysis.

B. MASS BALANCE:

The mass balance at the end of the adsorption phase of the study at the highest concentration was 97.8, 91.8, 93.3, and 93.3 percent of the applied radioactivity in the sandy loam, silt loam, sand and loam sediments, respectively. The mass balance at the end of the desorption phase was 99.9, 93.8, 96.3, and 98.7 percent of the applied radioactivity in the sandy loam, silt loam, sand and loam sediments, respectively.

Table 5: Recovery of [^{14}C]-CL 322,250 expressed as percentage of applied radioactivity, in sediment after adsorption/desorption (mean of two replicates)

Matrices	Sandy Loam (USDA classification) Code S 242	Silt Loam (USDA classification) Code S 243	Sand (USDA classification) Code S 241	Loam (USDA classification) Code S 244
At the end of the adsorption phase				
Supernatant solution	3.59	1.79	40.2	4.71
Solid phase (total ^{14}C)*	49.6	56.9	45.1	69.8
Non-extractable residues in sediment	44.6	33.1	7.98	18.8
Total recovery	97.8	91.8	93.3	93.3

Matrices	Sandy Loam (USDA classification) Code S 242	Silt Loam (USDA classification) Code S 243	Sand (USDA classification) Code S 241	Loam (USDA classification) Code S 244
At the end of the desorption phase				
Adsorption supernatant	3.4	1.75	40.5	4.49
Desorption supernatant	2.91	1.2	17.7	3.15
Solid phase (total ^{14}C)*	44.7	54.3	28.8	67.9
Non-extractable residues in sediment	48.8	36.5	9.36	23.2
Total recovery	99.9	93.8	96.3	98.7

* The amount on the sediment residue was calculated by difference.

Table 6: Concentration of [^{14}C]-CL 322,250 (expressed as R107894 equivalents) in the solid and liquid phases at the end of adsorption equilibration period (mean of two replicates).

	Fresh Water Sediments						Marine Sediments					
	Sandy Loam (USDA classification) Code S 242			Silt Loam (USDA classification) Code S 243			Sand (USDA classification) Code S 241			Loam (USDA classification) Code S 244		
Initial Solution Concentration (ng equiv/g)	on sediment[1] (ng equiv/g)	in solution (ng equiv/g)	% adsorbed[2]	on sediment[1] (ng equiv/g)	in solution (ng equiv/g)	% adsorbed[2]	on sediment[1] (ng equiv/g)	in solution (ng equiv/g)	% adsorbed[2]	on sediment[1] (ng equiv/g)	in solution (ng equiv/g)	% adsorbed[2]
Control												
433	2078	15.7	96.37	2118	7.97	98.16						
248	1197	8.76	96.47	1222	4.27	98.29						
100	485	3.02	96.99	493	1.43	98.57						
51	249	1.39	97.27	253	0.66	98.71						
451							1317	188.8	58.14	2145	22.05	95.11
249							751	99.04	60.23	1185	11.56	95.36
90							275	34.97	61.15	432	4.12	95.42
50							168	16.47	67.07	240	2.1	95.81

[1] The amount on the sediment residue was calculated by difference.
[2] Percentage adsorbed expressed as the percentage of the initial radioactivity applied.

Table 7: Concentration of [^{14}C]-CL 322,250 (expressed as R107894 equivalents) in the solid and liquid phases at the end of 16 hour desorption (mean of two replicates)

	Fresh Water Sediments						Marine Sediments					
	Sandy Loam (USDA classification) Code S 242			Silt Loam (USDA classification) Code S 243			Sand (USDA classification) Code S 241			Loam (USDA classification) Code S244		
Initial Solution Concentration (ng equiv/g)	on sediment[1] (ng equiv/g)	in solution (ng equiv/g)	% desorbed as % of the adsorbed	on sediment[1] (ng equiv/g)	in solution (ng equiv/g)	% desorbed as % of the adsorbed	on sediment[1] (ng equiv/g)	in solution (ng equiv/g)	% desorbed as % of the adsorbed	on sediment[1] (ng equiv/g)	in solution (ng equiv/g)	% desorbed as % of the adsorbed
Control												
433	2015	13.27	3.15	2092	5.53	1.3						
248	1166	6.54	2.68	1208	2.92	1.18						
100	476	1.98	2	490	0.85	0.85						
51	245	0.92	1.82	251	0.4	0.78						
451							929	85.43	18.52	2075	15.25	3.5
249							543	46.05	18.37	1149	7.97	3.3
90							198	17.09	18.87	418	2.84	3.22
50							131	8.13	16.08	234	1.34	2.76

[1] Each value in the solid phase is the amount present after 16 hour desorption and each value in the solution phase is the total amount desorbed.

Table 8: Adsorption and desorption constants of [^{14}C]-CL 322,250 in the sediments.

	Sediment	Adsorption				Desorption			
		K_a or K	1/N	R^2	K_{oc}	K_a	1/N	R^2	K_{oc}
Fresh Water Sediments	Sandy Loam (USDA classification) Code S 242	K=189 K_a = 132-179	0.864	1	6000-8136	K_a = 152-266			6887-12091
	Silt Loam (USDA classification) Code S 243	K=357 K_a = 266-383	0.859	1	13275-19150	K_a = 379-635			18950-31725
Marine Sediments	Sand (USDA classification) Code S 241	K=14 K_a = 7-10	0.857	0.998	1000-1429	K_a = 37940			1571-2286
	Loam (USDA classification) Code S 244	K=119 K_a = 97-114	0.935	1	2772-3257	K_a = 136-174			3886-4972

K_a -Adsorption and desorption coefficients
K - Freundlich adsorption and desorption coefficients
1/N -Slope of Freundlich adsorption/desorption isotherms
K_{oc} - Coefficient adsorption per organic carbon (K_d or K x 100/% organic carbon)
R^2 - Regression coefficient of Freundlich equation

C. ADSORPTION:

After 16 hours of equilibration, 96.4, 96.5, 97.0, and 97.3 percent of the applied radioactivity (expressed as R107894 equivalents) was adsorbed in sandy loam sediment at initial concentrations of 433, 248, 100, and 51 ng equiv/g, respectively. After 16 hours of equilibration, 98.2, 98.3, 98.6, and 98.7 percent of the applied radioactivity was adsorbed in silt loam sediment at initial concentrations of 433, 248, 100, and 51 ng equiv/g, respectively. After 16 hours of equilibration, 58.1, 60.2, 61.2, and 67.1 percent of the applied radioactivity was adsorbed in sand sediment at initial concentrations of 451, 249, 90, and 50 ng equiv/g, respectively. After 16 hours of equilibration, 95.1, 95.4, 95.4, and 95.8 percent of the applied radioactivity was adsorbed in loam sediment at initial concentrations of 451, 249, 90, and 50 ng equiv/g, respectively. The adsorption Freundlich constants were K_f = 189 (1/n = 0.864) in sandy loam, K_f = 357 (1/n = 0.859) in silt loam, K_f = 14 (1/n = 0.857) in sand, and K_f = 119 (1/n = 0.935) in loam sediments.

The adsorption coefficient K_a values ranged from 132 to 179 in sandy loam, 266 to 383 in silt loam, 7 to 10 in sand, and 97 to 114 in loam sediments. The adsorption K_{oc} values ranged from 6000 to 8136 in sandy loam, 13275 to 19150 in silt loam, 1000 to 1429 in sand, and 2772 to 3257 in loam sediments.

D. DESORPTION:

After 16 hours of equilibration, 3.15, 2.68, 2.00, and 1.82 percent of the adsorbed radioactivity was desorbed in sandy loam sediment at initial concentrations of 433, 248, 100, and 51 ng equiv/g, respectively. After 16 hours of equilibration, 1.30, 1.18, 0.85, 0.78 percent of the adsorbed radioactivity was desorbed in silt loam sediment at initial concentrations of 433, 248, 100, and 51 ng equiv/g, respectively. After 16 hours of equilibration, 18.5, 18.4, 18.9, and 16.1 percent of the adsorbed radioactivity was desorbed in sand sediment at initial concentrations of 451, 249, 90, and 50 ng equiv/g, respectively. After 16 hours of equilibration, 3.50, 3.30, 3.22, and 2.76 percent of the adsorbed radioactivity was desorbed in loam sediment at initial concentrations of 451, 249, 90, and 50 ng equiv/g, respectively.

The desorption coefficient K_d values ranged from 152 to 266 in sandy loam, 379 to 635 in silt loam, 11 to 16 in sand, and 136 to 174 in loam sediments. The desorption K_{oc} values ranged from 6887 to 12091 in sandy loam, 18950 to 31725 in silt loam, 1571 to 2286 in sand, and 3886 to 4972 in loam sediments. The desorption K_d and K_{oc} values were higher than those obtained for adsorption.

The desorption K_d and K_{oc} values were higher than those obtained for adsorption.

III. STUDY DEFICIENCIES:

There were a few issues of concern with the study. They are as follows:

- No control solutions were tested in the study.
- Complete sediment properties and storage conditions were not reported.
- The three sediments selected were slightly different than those recommended by the guidelines.

These issues did not appear to affect the validity of the study.

IV. REVIEWER'S COMMENTS: None

V. REFERENCES: None provided.

Conclusion: RASSB concludes that this missing information does not alter the acceptability of the study. The study is acceptable.

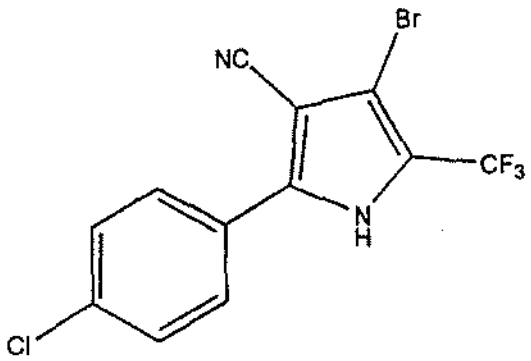
ATTACHMENTS:

1. Structure of [^{14}C]-R107894 and Hydrolysis Products

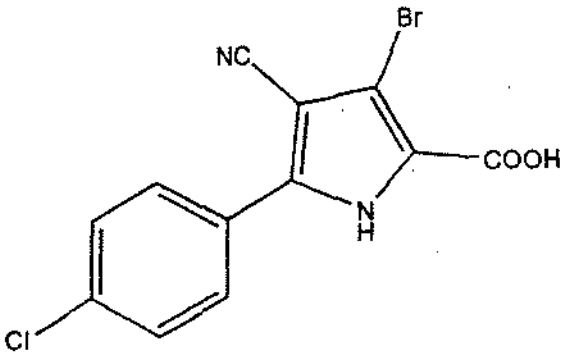
ATTACHMENT 1

Structure of R107894 and Putative Hydrolysis Products

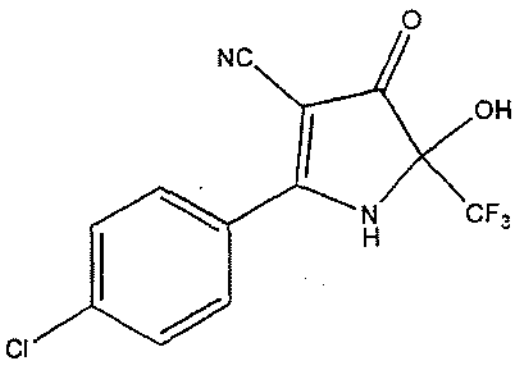
R107894



CL 322,250



CL 325,195



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 22, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Review of Aerobic Degradation Study for ECONEA™ Technical Containing AC 303268 Antifoulant

TO: Marshall Swindell, Product Manager, Team 33
Regulatory Management Branch I
Antimicrobials Division (7510C)

FROM: Srinivas Gowda, Microbiologist/Chemist Srinivas Gowda 1/22/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

THRU: Siroos Mostaghimi, Acting Team Leader, Team One
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

Norm Cook, Chief 1/28/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

DP Barcodes: D289027
Decision #: 220066
Case Type: New Registration
PC Codes: 119093
Chemical Name: 1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

EPA File Symbol: 43813-ET
MRID No.: 456739-11 & 456739-12
Data Submitter: Janssen Pharmaceutica Inc.
CAS#: 122454-29-9
Common Name: AC303268

INTRODUCTION:

Janssen Pharmaceutica Inc. has submitted the aerobic degradation study for the active ingredient 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- (also known as AC 303268) to meet the U.S. Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide Assessment Guidelines, Subdivision N, § 162-4 in support of new registration of ECONEA™ Technical, EPA File Symbol 43813-ET, for formulation of antifouling treatment products. The submitted aerobic degradation study has undergone review by Srinivas Gowda of Antimicrobials Division's Risk Assessment and Science Support Branch.

BACKGROUND:

1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- is a new active ingredient in ECONEA™ Technical Anti-fouling Preservative. It is also known as AC303268.

CONCLUSIONS:

1a. In the fresh water silt loam system, DT_{50} was estimated as being between 3 and 7 days and the DT_{90} was estimated as being just over 30 days.

1b. In the marine water sandy loam system, DT_{50} was estimated as being less than 1 day and DT_{90} was estimated as approximately 7 days.

2a. The two major transformation productd were CL 322,250 and Unknown B.

2b. The minor transformation products were 325,195, Unknown A, Unknown C, and Unknown D.

RECOMMENDATIONS:

This study is classified as acceptable and satisfies the guideline requirement for aerobic biotransformation study in two water-sediment systems. RASSB recommends that the aerobic degradation study for AC 303268 be accepted in support of ECONEA™ Technical MUP registration.

AEROBIC BIOTRANSFORMATION OF [^{14}C]-R107894 IN TWO WATER/SEDIMENT SYSTEMS

DATA EVALUATION REPORT

PRODUCT FORMULATION: ECONEA™ Technical Anti-Fouling Preservative

ACTIVE INGREDIENT: 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl), also known as AC 303268

BACKGROUND: The study was submitted to evaluate the aerobic degradation of the active ingredient AC 303268 in two freshwater and two marine sediments. The study was conducted according to the Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide

Assessment Guidelines, Subdivision N, § 162-4.

CITATION:

Study Title:	"The Aerobic Degradation of [^{14}C]-R107894 in Two Water/Sediment Systems"
Report Date:	February 15, 1999
Author:	J A Mackie Study Director
Laboratory Name:	Inveresk Research Tranent, EH33 2NE Scotland
Laboratory Report No.:	16787
Sponsor:	Janssen Pharmaceutica N.V. Turnhoutseweg 30 B-2340 Beerse Belgium

OPPTS GUIDELINE NO.: Subdivision N, 162-4

EXECUTIVE SUMMARY:

The biotransformation of radiolabelled R107894 was studied in a freshwater/sediment system (water pH 6.5, silt loam, organic carbon 2.5%) and a marine water/sediment system (water pH 8.04, sandy loam, pH 7.53, organic carbon 0.8%) collected from Bogton Loch and Seaby Bay in Scotland. The experiment was performed for 30 days under aerobic conditions in the dark at 21°C. Radiolabelled R107894 was applied at the rate of 0.5 mg/L. The experiment was conducted in accordance with the Pesticide Assessment Guidelines, Subdivision N, Section 162-4, and in compliance with GLP standards as specified in 40 CFR Part 160. The test system consisted of borosilicate glass cylinders (previously silanised; 15.9 cm^2 cross-sectional area) as the incubation vessel and included a series of three traps for trapping non-specific [^{14}C]-organic volatiles and liberated $^{14}CO_2$. Samples were collected at 0, 2 hours, and 1, 3, 7, 15, and 30 days of incubation. The water samples were not extracted. The sediment samples were extracted twice with 50 ml of acetonitrile and then shaken for 1 hour, followed by centrifugation for 15 minutes. Quantification and identification of the [^{14}C]-R107894 residues was performed using TLC and HPLC.

For the silt loam (freshwater) test system, the mean overall recovery of radiolabelled material was 93.8 ± 5.2% of the applied amount. For the loamy sand (marine water) test system, the mean overall recovery of radiolabelled material was 95.5 ± 4.4% of the applied amount.

The concentration of the parent compound in freshwater immediately after the application showed a mean of 51.2% of the applied amount and had dropped below the detection limit by the end of the study period (Day 30). The concentration of the parent compound in the silt loam (freshwater) sediment decreased from a mean of 36.3% of the applied amount at Day 0 to a mean of 16.4% of the applied amount at the study termination. The concentration of the parent compound in marine water decreased from a mean of 77.2% of the applied amount at Day 0 to

below the detection limit by Day 15 of the study. The concentration of the parent compound in loamy sand (marine) sediment decreased from a mean of 18.05% of the applied amount at Day 0 to a mean of 4.04% by Day 7.

The DT50 and DT90 values were estimated by visual inspection of the data by the Registrant. The DT50 for [^{14}C]-R107894 in the freshwater silt loam system was estimated as being between 3 and 7 days and the DT90 was estimated as being just over 30 days. In the marine water loamy sand test system, the DT50 and DT90 were estimated as being less than 1 day and approximately 7 days, respectively. The two major transformation products were CL 322,250 and Unknown B (a supplementary study tentatively identified this component as debrominated CL 322,250). There were four minor transformation products. These minor transformation products were referred to as CL 325,195, Unknown A, Unknown C, and Unknown D.

For the silt loam sediments, extractable ^{14}C-residues decreased from a mean of 38.1% of the applied amount at Day 0 to a mean of 26.2% of the applied amount at study termination. Non-extractable [^{14}C]-residues increased from a mean of 1.82% of the applied amount at Day 0 to a mean of 36.43% of the applied amount at the end of incubation period. For the loam sand sediments, extractable ^{14}C-residues increased from a mean of 21.4% of the applied amount at Day 0 to a mean of 33.7% of the applied amount at study termination. Non-extractable [^{14}C]-residues increased from a mean of 0.275% of the applied amount at Day 0 to a mean of 6.54% of the applied amount at the end of the incubation period.

For the freshwater silt loam sediment system, there were no detectable levels of radioactivity present as CO_2 or volatile compounds at the end of the study. For the marine water loamy sand sediment system, a mean of 0.02% of the recovered radioactivity was present as CO_2. Volatile compounds were not detectable.

Results Synopsis:

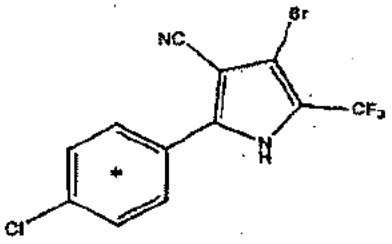
Test systems used:	Freshwater/silt loam sediment and marine water/sandy loam sediment In the fresh water/silt loam system, DT50 was estimated as being between 3 and 7 days.
Half-life:	In the marine water/sandy loam system, DT50 was estimated as being less than 1 day.
Major transformation products:	CL 322,250 and another unidentified component (Unknown B)
Minor transformation products:	CL 325,195 and two other unidentified components (Unknowns A, C, and D)

Study Acceptability: This study is classified acceptable and satisfies the guideline requirements for an aerobic biotransformation study in soil. The deficiencies and points of concern are noted in this study review.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The guidelines followed for this study were from the U.S. Pesticide Assessment Guidelines, Subdivision N, Environmental Fate:Aerobic Aquatic Metabolism Series 162-4.

COMPLIANCE: The study was conducted in compliance with GLP Standards as specified in 40 CFR Part 160. A signed GLP statement was provided which confirmed compliance with no exceptions. A Quality Assurance Statement and a DataConfidentialityStatement were also provided in the Study Report.



* = Position of Carbon-14 Label

A. MATERIALS

1. Test Material:

Chemical: [^{14}C]-R107894

Chemical Structure:

Description: The test substance was supplied as a liquid.

Radiochemical purity: The stated radiochemical purity of the test substance was >99%. The radiochemical purity of the test substance was determined by TLC and HPLC. The mean radiochemical purity of the test substance was 97.37%.

Lot/Batch No.: Lot# 101-077-026 (radiolabelled R107894)
Batch # AC6943-27 (non-radiolabelled R107894)

Specific activity: The stated specific activity was 26.4 mCi/mmol (75.4 µCi/mg).

Locations of the radio label: The radio label was evenly distributed within the carbon ring.

Storage conditions of test chemicals: The test solutions were stored at approximately -20°C in the dark.

Physico-chemical properties of [^{14}C]-R107894: Water solubility, vapor pressure/volatility, UV absorption, pK_a, K_{ow}/log K_{ow}, and stability of the compound at room temperature were not provided in the Study Report.

2. Water and Sediment Characteristics:

Water/Sediment collection and storage: See Table 1.

Table 1: Description of Water-Sediment Collection and Storage

Description		Fresh water/sediment	Marine water/sediment
Geographic location		Bogton Loch, Scotland; Wetlands, agrochemical free catchment	Raw sea water supplied from Flotta laboratory supply in Scotland. Sediment was collected from Seaby Bay in Scotland.
Pesticide use history at the collection site		Not reported	Not reported
Collection procedures for	water:	Not reported	Study says the water was pumped from Scapa Flow at the Flotta laboratory.
	sediment:	Not reported; 12 kg of sediment collected	Not reported
Sampling depth for	water:	54 cm	Water and sediment were collected from different sources. Water was pumped. Depth of water adjacent to the sediment was 10 cm.
	sediment:	0-30 mm	
Storage conditions		4°C in the dark under aerobic conditions prior to use	
Storage length		The test samples were pre-incubated for 7 days in the dark. Total length of storage for each sample was not reported.	
Preparation of water and sediment samples (eg: water -filtered/not filtered; sediment -sieved/not sieved)		Water was filtered through a 0.2 mm sieve prior to supply. Sediment was passed through a 2 mm sieve prior to delivery.	Water was passed through a 171 µm mesh. Sediment was sieved through a 600 µm mesh. The sediment was exposed at low tide.

Water Properties: See Table 2.

Table 2: Properties of the Water

Property	Fresh water		Marine water	
Temperature (°C)	13.5		10	
pH	6.5		8.04	
Redox potential (mV)[a]	Initial	Final	Initial	Final
	125	53.5	56.5	68.5
Oxygen concentration (%)[b]	Initial	Final	Initial	Final
	94.5	73	74	55.5
Dissolved organic carbon (mg/L)	13.4		174.3	
Hardness (mg/L $CaCO_3$)	39		7100	
Electrical conductivity (µS/cm)	37		>1500	
Biomass (mg microbial C/100 g or CFU or other)	Not reported		Not reported	

a - An initial redox potential of 238 mV was reported by the supplier for the freshwater. Initial and final redox potentials presented in table are averages of measurements taken from two control replicates for each water/sediment system type throughout the duration of the study.
b - Averages of measurements taken from two control replicates.

Sediment Properties: See Table 3.

Table 3: Properties of the Sediment

Property	Fresh water sediment		Marine water sediment	
Textural classification (according to USDA, 1995)	Silt Loam		Sandy Loam	
% sand	22.07		83.28	
% silt	55.92		13.75	
% clay	22.01		2.97	
pH	5.8[a]		7.7	
Organic carbon (%)	2.5		0.8	
CEC (meq/100 g)	18.3		5.2	
Redox potential[b] (mV)	Initial	Final	Initial	Final
	125	53.5	56.5	68.5
Bulk density (g/cm^3)	Not reported		Not reported	
Biomass (mg microbial C/100 g or CFU or other)	Not reported		Not reported	

a pH in water (1:5).
b Initial and final redox potentials presented in table are average of measurements taken from two control replicates for each water/sediment system type throughout the duration of the study.

B. EXPERIMENTAL CONDITIONS

1. Preliminary Experiments:

Testing for Adsorption to Glassware:

During a preliminary study, [^{14}C]-R107894 was dissolved in acetonitrile and dispensed into a variety of silanised and non-silanised glass vessels. The vessels contained either Milli-Q grade water or acetonitrile. The levels of radioactivity in these solutions were determined immediately following the addition of [^{14}C]-R107894 and the following day. No adsorption to glassware was observed for any of the glass vessels.

2. Experimental Conditions: See Table 4.

Table 4: Study Design

Criteria		Fresh water/sediment system	Marine water/sediment system
Duration of the test		30 Days	30 Days
Water: Filtered/unfiltered water: Type and size of filter used, if any:		Fresh water was filtered through a 0.2 mm sieve	Raw sea water was filtered through a 171 µm mesh.
Amount of sediment and water per treatment		110 mL of silt loam surface water was added to 11 g of silt loam.	150 mL of sea water was added to 15 g of loamy sand.
Sediment/water ratio		1 g : 10 mL	1 g : 10 mL
Application rates (mg a.i./L)		0.5	0.5
Control conditions, if used (present differences from other treatments, i.e., sterile/non-sterile, experimental conditions)		Two additional units were prepared in incubation vessels to be used as controls. Non-labelled R107894 was added to these.	Two additional units were prepared in incubation vessels to be used as controls. Non-labelled R107894 was added to these.
No. of replications	Control, if used:	2	2
	Treatments:	2	2
Test apparatus (Type/material/volume)		Silanised borosilicate glass cylinders with 15.9 cm^2 cross sectional area.	
Details of traps for CO_2 and volatile organics, if any		Safety trap: filled with polyurethane plugs to trap non-specific ^{14}C-organic volatiles. Second trap: contained ethanediol to trap non-specific ^{14}C-organic volatiles. Third trap: contained ethanolamine to trap liberated $^{14}CO_2$.	
Identity and concentration of co-solvent		None reported	None reported

Criteria		Fresh water/sediment system			Marine water/sediment system	
Test material application	Volume of the test solution used/treatment:	100 µL of test solution containing 54.6 µg [^{14}C]-R107894 for all samples except for zero time and 2 hour sampling interval. 100 µL of test solution containing 57.8 µg [^{14}C]-R107894 for zero time and 2 hour sampling intervals which were collected from a repeat application.			100 µL of test solution containing 73.7 µg [^{14}C]-R107894 for all samples except for zero time and 2 hour sampling interval. 100 µL of test solution containing 74.6 µg [^{14}C]-R107894 was used for zero time and 2 hour sampling intervals which were collected from a repeat application.	
	Application method (eg: mixed/not mixed etc.)	Applied to the surface of the water.			Applied to the surface of the water.	
Any indication of the test material adsorbing to the walls of the test apparatus		No adsorption to glassware was observed for any of the glass vessels.				
Microbial biomass/microbial population of the control[a]			Initial	Final	Initial	Final
		water: bacteria spores	2.21x10^4 0	696 0	3.3x10^4 43.3	4.4x10^4 1.65
		sediment: bacteria spores	2.2x10^5 1.15x10^4	2.8x10^5 1.96x10^5	1.36x10^6 4.6x10^4	7.45x10^5 4.05x10^4
Microbial biomass/microbial population of the treated[a]		See footnote.				
Experimental conditions:	Temperature (°C)	21			21	
	Continuous darkness (Yes/No)	Yes			Yes	
Other details, if any						

a - Viable bacterial estimations were provided for both aerobic and anaerobic conditions. It is not certain if these counts were from the control test systems or the treated test systems. The values presented in this table are for aerobic conditions only. Final bacteria and spore counts represent the average of two replicates.

3. Aerobic Conditions:

To maintain aerobic conditions, a stream of moist, CO_2-free air was introduced into the test systems via a dip tube extending to just below the water surface. Two additional units of each sediment type, used as controls, were prepared in incubation vessels to measure the redox potential and the oxygen concentration of the surface water during the incubation period. The redox potential was measured using a platinum combination redox electrode.

4. Supplementary Experiments:

A supplementary study entitled, "Identification of Unknown Component Present in a Day 30 Surface Water Following Application of [^{14}C]-R107894 to Loamy Sand Sediment" was performed. The supplementary study had no claim of confidentiality and was performed in

accordance with the requirements of GLP compliance. The Inveresk Report Number is 17802 and the report was dated October 19, 1999. One of the major transformation products from the Inveresk Report Number 16787 study was labeled as Unknown B and it had a retention time of approximately 26 minutes following the analysis of samples generated by the loamy sand (marine) test system.

For this supplementary study, two water samples from Day 30 were taken and concentrated by solid phase extraction. The concentrated samples were analyzed by negative ion electrospray liquid chromatography mass spectrometry in addition to radiochemical detection.

5. Sampling: See Table 5.

Table 5. Sampling Details

Parameters	Details
Sampling intervals	Samples were collected on day 0, 2 hours, and then on 1, 3, 7, 15, and 30 days after dosing
Sampling methods	Duplicate incubations from each sediment type were sampled. Method of sampling water and sediments were not provided.
Method of collection of CO_2 and volatile organic compounds	Traps were sampled and replenished at regular intervals throughout the incubation period. Ethanediol was used to trap non-specific [^{14}C]-organic volatiles and ethanolamine was used to trap liberated $^{14}CO_2$.
Sampling intervals/times for:	
sterility check:	Not mentioned
oxygen concentration:	Checked at each sampling interval.
redox potential/other:	Checked at each sampling interval.
Sample storage before analysis	Not mentioned
Other observations, if any	

C. ANALYTICAL METHODS

1. Separation of the Sediment and Water:

Surface waters were separated from the sediments by carefully decanting the water into amberlite jars and then transferring the sediments into separate amberlite jars.

2. Extraction/Clean Up/Concentration Methods:

Sediments: Sample extraction was performed twice by adding 50 ml of acetonitrile and then shaking for approximately 1 hour using an end over end shaker. After the extraction, the extract was separated from the residue by centrifugation at 1,000 rpm for 15 minutes. Aliquots of the subsequent extracts were combined and concentrated to 3 to 5 mL under a gentle stream of nitrogen at ambient temperature or by rotary evaporation under reduced pressure at 35 to 40°C. The radioactivity in the supernatant was determined by liquid scintillation counting. Following the extraction, the residues were subjected to combustion analysis to quantify residual radioactive content.

Surface water: Following decanting, aliquots of surface water were submitted for liquid scintillation counting. The remainder of each surface water was acidified to approximately a pH of 3 using 2 M hydrochloric acid, prior to storage to prevent hydrolysis of R107894. Because R107894 could have possibly precipitated out of solution, 25 mL of acetonitrile was added to each surface water sample. Aliquots of each sample were submitted for liquid scintillation counting.

3. Non-Extractable Residue Determination:

Following the extraction of the sediment samples, the residues were subjected to combustion analysis to quantify residual radioactive content. Triplicate portions of sediment residues, approximately 0.3 g each, were mixed with cellulose powder and 100 to 200 µL of Combustaid® before combusting in oxygen using a Packard Sample Oxidizer, Model 306. The combusted products were absorbed in Carbo-Sorb® mixed with Permafluor® V and the radioactivity was determined by liquid scintillation counting. A [^{14}C] standard was combusted at the beginning of each day and at regular intervals throughout the day to check combustion and trapping efficiencies.

4. Total ^{14}C Measurement:

Total [^{14}C] was reported to be the summation of the total extractable [^{14}C]-activity (surface water and sediments), total $^{14}CO_2$, total volatile [^{14}C]-activity, total [^{14}C]-non-extractable residues, and total [^{14}C]-activity found in the apparatus wash. The analysis methods for total sediment extractable and total non-extractable residues were provided above. Aliquots of surface waters, extracts, apparatus washes, and ethanediol and ethanolamine trap contents were added directly to the scintillant and counted by liquid scintillation counting. All radioassays were performed in duplicate.

Measurements of radioactivity were made using a liquid scintillation analyzer (Packard Tri-Carb 1600 TR, Packard Instruments) with automatic quench correction by external standard-channels ratio. Each individual sample was counted for 5 minutes. The vials were allowed to heat and light stabilize prior to analysis. Prior to calculation of each result, a background count rate was determined and subtracted from each sample count rate.

5. Derivatization Method, if used:
Not used.

6. Identification and Quantification of Parent Compound:
TLC and HPLC were both used for the quantification and identification of [^{14}C]-R107894.

For the TLC system, aliquots of up to 80 µL of each sample were analyzed using a silica gel 60F_{254} TLC plate and then developed in toluene:acetone:methanol:acetic acid (75:30:6:0.5 by volume). The solvent was allowed to develop to a height of 170 mm. Non-radiolabelled R107894, CL 322,250, and CL 325,195 were chromatographed under each sample. Following chromatography, quantification of radioactivity present on TLC plates was performed using a Molecular Dynamics phosphor imager. The standards were visualized by irradiation with ultraviolet light (254 nm).

For HPLC, a Hewlett-Packard 1050 series HPLC equipped with an autosampler, ultraviolet detector (set at 280 nm) and a solvent programmer, connected to an Inertsil Phenyl guard and HPLC column (1 cm and 25 cm x 4.6 mm; 5 µm; Hichrom) and a Packard Flo-One A-100 Series radioactivity monitor or a Berthold LB 507A radioactivity monitor. Data was collected by means of Labsystems Vax Multichrom 2, version 2.0, data handling system. A flow rate of 1.0 ml/minute was used with a gradient system using acetonitrile and 0.01 M sodium citrate buffer at a pH of 4. Non-radiolabelled reference standards were dissolved in acetonitrile:water (6:4, v/v) and injected onto the HPLC column individually and as a mixture to determine standard retention times. Surface water and sediment extract samples were admixed with a mixture of reference standards and injected onto the HPLC. Quantification of radioactivity was performed by integrating the area under each peak. According to the Study Report, the TLC data was similar to HPLC data and because the HPLC had greater resolution, the results provided were based on the results from the HPLC analyses.

7. Identification and Quantification of Transformation Products:
Characterization of radioactivity in surface waters and sediment extracts was carried out using both HPLC and TLC. TLC co-chromatography of the standard with the radioactivity was used for the tentative identification of degradation products. According to the Study Report, the TLC data was similar to HPLC data and because the HPLC had greater resolution, the results provided were based on the results from the HPLC analyses. A number of unidentified components were detected in both chromatographic systems and, where appropriate, the Study Report gave these components the same peak identifiers as were reported in other Inveresk reports (Inveresk 390042, 3907232, and 390770).

8. Detection Limits (LOD, LOQ) for the Parent Compound:
Neither a limit of detection (LOD) nor a limit of quantitation (LOQ) were provided for the parent compound. According to the Study Report, a limit of reliable determination of 30 d.p.m. above background count rate was instituted. Extracts and surface water samples were not chromatographed if they contained <10% of the applied radioactivity.

7. Detection Limits (LOD, LOQ) for the Transformation Products:
LODs and LOQs for the transformation products were not reported.

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS:

Aerobicity was maintained throughout the study. This was evidenced by the four control samples (two of each sediment type) which were monitored for oxygen content and redox potential for the duration of the study. The percent oxygen and redox potentials reported for time zero and 2 hour sampling intervals were those from the original test material application. These two sampling intervals were repeated due to R107894 hydrolysis in the surface water samples during the first application. The problem was corrected by the Day 1 sampling interval and therefore, only the first two sampling intervals needed to be repeated. There were no control samples for this repeated application. For the silt loam (freshwater system), the average percent oxygen and average redox potential at the zero time sampling interval was 94.5% and 125 mV, respectively. The average percent oxygen and average redox potential at the Day 30 sampling interval was 73% and 53.5 mV, respectively. For the loamy sand (marine water system), the average percent oxygen and average redox potential at the zero time sampling interval was 74% and 56.5 mV, respectively. The average percent oxygen and average redox potential at the Day 30 sampling interval was 55.5% and 68.5 mV, respectively. Daily temperature data were not provided for the two systems but according to the Study Report, the systems were kept at 21°C in the dark for the duration of the study. Total viable aerobic and anaerobic bacterial estimations were provided for the sediments and the surface waters (pre- and post-study). For the silt loam sediments, a pre-study aerobic bacteria and spore count of 2.2×10^5 and 1.15×10^4, respectively, and an average post-study count of 2.8×10^5 and 1.96×10^5, respectively, were reported. For the loamy sand sediments, a pre-study aerobic bacteria and spore count of 1.36×10^6 and 4.6×10^4, respectively, and an average post-study count of 7.45×10^5 and 4.05×10^4, respectively, were reported. For the freshwater, a pre-study aerobic bacteria count of 2.21×10^4 with no spores and an average post-study aerobic bacteria count of 696 with no spores, were reported. For the marine water, a pre-study aerobic bacteria and spore count of 3.3×10^4 and 43.3, respectively, and an average post-study count of 4.4×10^4 and 1.65, respectively, were reported.

B. MATERIAL BALANCE:

For the silt loam (freshwater) test system, the total mean recovery of radiolabelled material ranged from 87.8 to 96.9% of the applied amount. The mean overall recovery was 93.8 ± 5.2% of the applied amount. For the loamy sand (marine water) test system, the total mean recovery of radiolabelled material ranged from 89.2 to 101% of the applied amount. The mean overall

recovery was 95.5 ± 4.4% of the applied amount. Tables 6 and 7 provide biotransformation as a percentage of applied radioactivity in the two water-sediment systems under aerobic conditions (freshwater/silt loam sediment and marine water/loamy sand sediment).

Table 6: Biotransformation of [^{14}C]-R107894, Expressed as Percentage of Applied Radioactivity in Freshwater / Silt Loam Sediment Under Aerobic Conditions

Compound		Sampling times (days)						
		0	0.083 (2 hours)	1	3	7	15	30
Parent compound	water	51.2	66.7	48.2	34.5	11.4	6.3	ND
	sediment	36.3	5.44	30.4	44.5	23.5	39.3	16.4
CL 322,250	water	ND	ND	7.1	7.4	48.2	30.6	33.3
	sediment	ND	ND	ND	ND	3.87	3.99	7.85
CL 325,195	water	ND	ND	ND	ND	ND	ND	ND
	sediment	ND	ND	ND	0.38	ND	0.38	ND
Unknown A	water	ND	ND	ND	ND	ND	ND	ND
	sediment	0.87	ND	2.02	3.59	0.84	1.17	1.15
Unknown C	water	ND	1.1	ND	ND	ND	ND	ND
	sediment	0.925	ND	ND	0.3	0.635	1.27	0.845
Total CO_2	entire system	NS	ND	ND	0	0.01	0.06	ND
Total volatile organics	entire system	NS	ND	ND	ND	ND	ND	ND
Non-extractable residues	sediment	1.82	0.475	1.72	4.08	7.74	10.9	36.4
Apparatus Wash	entire system	0.215	9.89	1.37	1.98	0.725	1.69	0.38
Total % recovery	water	51.2	67.6	56.4	41.9	59.6	36.9	33.3
	sediment	38.1	9.58	32.4	48.8	28.9	46.1	26.2
	entire system	91.3	87.8	91.8	96.7	96.9	95.7	92.3

Note: All values based on the average of duplicate samples for each sampling interval analyzed by HPLC.
ND - Not detected; a detection limit was not provided.
NS - No sample

Table 7: Biotransformation of [^{14}C]-R107894, Expressed as Percentage of Applied Radioactivity in Marine Water / Loamy Sand Sediment Under Aerobic Conditions

Compound		Sampling times (days)						
		0	0.083 (2 hours)	1	3	7	15	30
Parent compound	water	77.2	64.9	15.6	8.5	5.29	ND	ND
	sediment	18.1	NP	NP	4.96	4.04	15.8	15.3
CL 322,250	water	ND	21	64.3	68.1	71.9	45.4	33.8
	sediment	0.795	NP	NP	0.92	3.72	5.22	4.33
CL 325,195	water	ND	ND	ND	ND	ND	ND	ND
	sediment	1.1	NP	NP	NP	ND	0.475	1.87
Unknown A	water	0.815	4.02	ND	ND	ND	ND	ND
	sediment	0.635	NP	NP	NP	ND	0.47	ND
Unknown B	water	ND	ND	ND	1.11	4.07	8	19.5
	sediment	ND	NP	NP	NP	3.79	9.55	10.8
Unknown C	water	ND	0.96	ND	1.71	ND	ND	ND
	sediment	0.24	NP	NP	NP	0.355	0.335	0.805
Unknown D	water	ND	ND	ND	ND	ND	ND	ND
	sediment	0.59	NP	NP	NP	ND	0.97	0.505
Total CO_2	entire system	NS	ND	ND	ND	ND	0.01	0.02
Total volatile organics	entire system	NS	ND	ND	ND	ND	ND	ND
Non-extractable residues	sediment	0.275	0.495	1.13	2.51	3.19	5.76	6.54
Apparatus Wash	entire system	0.16	0.865	1.35	0.27	0.355	0.65	2.27
Total % recovery	water	78	90.9	79.9	79.4	81.2	53.4	53.3
	sediment	21.4	9.2	6.84	10.6	11.9	32.8	33.7
	entire system	99.9	101	89.2	92.7	96.7	92.7	95.8

Note: All values based on the average of duplicate samples for each sampling interval analyzed by HPLC.
ND - Not detected; a detection limit was not provided.
NP - Not profiled (samples contained <10% of applied radioactivity)
NS - No sample

C. TRANSFORMATION OF PARENT COMPOUND:

The concentration of the parent compound in freshwater first increased from a mean of 51.2% of

the applied amount immediately after the application (Day 0) to a mean of 66.7% at the 2 hour sampling interval. The concentration then decreased to below the detection limit at the end of the study period (Day 30). The concentration of the parent compound in the silt loam sediment decreased from a mean of 36.3% of the applied amount at Day 0 to a mean of 16.4% of the applied amount at the study termination.

The concentration of the parent compound in marine water decreased from a mean of 77.2% of the applied amount at Day 0 to below the detection limit by Day 15 of the study. The concentration of the parent compound in loamy sand decreased from a mean of 18.05% of the applied amount at Day 0 to a mean of 4.04% by Day7. However, the concentration then increased to a mean of 15.8% on Day 15 and decreased to a mean of 15.3% by Day 30. At the 2 hour sampling interval the concentration of the parent compound was not profiled because the recoveries were less than 10% of the applied amount.

1. Half-life:

The Registrant originally calculated the rate of degradation of [^{14}C]-R107894 in each test system by linear regression analysis using the total percentage of parent present at each sampling interval (using the HPLC data) versus time. However, according to the Registrant, the data did not fit very well and as a result the DT50 and DT90 values were estimated by visual inspection of the data. The DT50 for [^{14}C]-R107894 in the freshwater silt loam system was estimated as being between 3 and 7 days and the DT90 was estimated as being just over 30 days. In the marine water loamy sand test system the DT50 and DT90 were estimated as being less than 1 day and approximately 7 days, respectively.

RASSB calculated half-life estimations based on the information provided in the report. First-order dissipation kinetics were assumed in generating dissipation curves using the mean percent recoveries of the parent compound dose in each test system out to the day prior to where the percentages dropped below the detection limit. The values used were based on the HPLC data. For the silt loam sediment, RASSB dropped the 2 hour sampling interval because it was an outlier. RASSB was unable to calculate a half-life for the loamy sand sediment because of insufficient information (no LOD or LOQ). Table 8 provides a summary of RASSB's estimated half-life calculations and the Registrant's visually estimated DT50 and DT90 for each test system.

Table 8. Half-life/DT50 and DT90 Values for [^{14}C]-R107894

System	Model	DT50 (Half-life)	DT90 (Interval)	Regression Equation	r^2
Registrant Calculated Values					
Fresh water	--	3 - 7 days	30 + days	NP[a]	NP
Marine	--	<1 days	7 days	NP	NP
Versar Calculated Values					
Fresh water	1st order regression	4.43 days	--	y = -0.156x + 3.985	0.932
sediment		31 days	--	y = -0.022x + 3.613	0.478
entire		13.5 days	--	y = -0.051x + 4.361	0.864
Marine water	1st order regression	1.95 days	--	y = -0.355x + 3.802	0.753
sediment		--[b]	--	--	--
entire		20.5 days	--	y = -0.034x + 3.385	0.181

a Not provided
b Could not be calculated; no detection limit provided
Note: Values based on mean percent of amount applied (HPLC data).

2. Transformation Products:

The major transformation product detected in the freshwater was CL 322,250, with a maximum concentration mean of 48.2% of the applied amount, observed on the 7th day of incubation. A concentration mean of 33.3% of the applied amount was observed on the last day of the study (Day 30). A minor transformation product detected in the freshwater was designated as Unknown C, with a single concentration mean of 1.11% of the applied amount, observed two hours after the test substance was applied. It dropped below the detection limit by Day 1.

The major transformation product detected in the silt loam sediment was CL 322,250, with a maximum concentration mean of 7.85% of the applied amount, observed on the 30th (last) day of incubation. Three minor transformation products detected in the silt loam sediment were CL 325,195 and two unknowns designated as Unknown A and Unknown C. CL 325,195 was observed twice at equal concentrations (0.380% of the applied amount) on the 3rd and 15th days of incubation. Unknown A and Unknown C were detected at maximum concentration means of 3.59% of the applied amount on the 3rd day and 1.27% of the applied amount on the 15th day, respectively. The corresponding concentrations in the silt loam sediment for these two minor transformation unknowns were 1.15% and 0.85% by the termination of the study (Day 30).

There were two major transformation products detected in the marine water. They were CL 322,250 and an unknown designated as Unknown B, with maximum concentration means of 71.9% and 19.5% of the applied amount, respectively, observed on the 7th and 30th days of incubation. The CL 322,250 concentration in the marine water at the end of the study period was 33.8% of the applied amount. Two minor transformation products detected in the marine water were designated as Unknown A and Unknown C, with maximum concentration means of 4.02%

and 1.71% of the applied amount, observed two hours after the test substance was applied and on the 3rd day of incubation, respectively. Both unknowns dropped below the detection limit by Day 1 and Day 7, respectively.

There were two major transformation products detected in the loamy sand sediment. They were CL 322,250 and an unknown designated as Unknown B, with maximum concentration means of 5.22% and 10.8% of the applied amount, observed on the 15th and 30th days of incubation, respectively. The CL 322,250 concentration in the loamy sand sediment at the end of the study period was 4.33% of the applied amount. Four minor transformation products detected in the silt loam sediment were CL 325,195 and three unknowns designated as Unknown A, Unknown C, and Unknown D. CL 325,195 had a maximum concentration mean of 1.87% of the applied amount which was observed on the 30th day of incubation. Unknowns A, C, and D were detected at maximum concentration means of 0.64%, 0.81%, and 0.97% of the applied amount which were observed on the 1st, 30th, and 15th days of incubation, respectively.

3. Extractable and Non-Extractable Residues:

For the silt loam sediments, extractable [^{14}C]-residues decreased from a mean of 38.1% of the applied amount at Day 0 to a mean of 26.2% of the applied amount at study termination. Non-extractable [^{14}C]-residues increased from a mean of 1.82% of the applied amount at Day 0 to a mean of 36.43% of the applied amount at the end of incubation period.

For the loam sand sediments, extractable [^{14}C]-residues increased from a mean of 21.4% of the applied amount at Day 0 to a mean of 33.7% of the applied amount at study termination. Non-extractable [^{14}C]-residues increased from a mean of 0.28% of the applied amount at Day 0 to a mean of 6.54% of the applied amount at the end of incubation period.

4. Volatilization:

For the freshwater silt loam sediment system, there were no detectable levels of radioactivity present as CO_2 or volatile compounds at the end of the study. For the marine water loamy sand sediment system, a mean of 0.02% of the recovered radioactivity was present for CO_2. Volatile compounds were not detectable.

5. Transformation Pathway:

The two major transformation products were CL 322,250 and Unknown B (supplementary study tentatively identified this component as debrominated CL 322,250). There were four minor transformation products. These minor transformation products were referred to as CL 325,195, Unknown A, Unknown C, and Unknown D. The biotransformation pathway was not provided in the Study Report.

D. SUPPLEMENTARY EXPERIMENT-RESULTS:

Two peaks were identified in the radiochromatogram during the supplementary study. The latter of these was confirmed as CL 322,250 by comparison of retention time, full scan spectrum and daughter spectrum to those obtained following the analysis of authentic CL 322,250. The first peak (Unknown B) was tentatively postulated as debrominated CL 322,250 based on comparison of retention times, spectra and daughter spectra for this peak and the CL 322,250 reference standard.

III. STUDY DEFICIENCIES:

The following study deficiencies were noted:

- The pH, water solubility, vapor pressure/volatility, UV absorption, pK_a, K_{ow}/log K_{ow}, and stability of the test substance at room temperature were not provided.
- A description of the procedures used for sampling surface waters and sediments and subsequent storage were not provided in the Study Report.
- The Study Report did not provide LOD or LOQ for the parent compound nor the transformation products.
- The Study Report did not provide biomass data for the waters or sediments.
- The Study Report did not provide the bulk density for the sediments.

IV. REVIEWER'S COMMENTS:

The following points of concern were noted:

- Raw data were not provided, therefore RASSB could not verify percentages presented in the Study Report.
- Total viable bacterial estimations were provided in the Study Report, however it is not certain if these values represent the treated or control test systems.
- The Study Report provided values for DT50 and DT90 but did not specify which data were used to calculate these values. It is assumed that these are decline times for the entire fresh water and marine test system.
- RASSB was unable to verify the values provided in the Study Report for both the fresh water and marine test systems. RASSB was able to calculate half-lives, based on a linear regression of the mean percent dose values, however, the half lives calculated for the entire systems are much higher than those reported by the Registrant. The registrant estimated their DT50 value, by visual inspection of the data, while RASSB's determination was based on a linear regression. RASSB was unable to calculate a half-life for the sediment compartment of the marine test system since several percent of dose values were reported as non-detect and a detection limit was not provided in the Study Report.

V. REFERENCES:

No references were cited in the Study Report.

Conclusion: RASSB concludes that this missing information does not alter the acceptability of the study. The study is acceptable.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 22, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Review of Hydrolysis Data for ECONEA™ Technical containing AC303268

TO: Marshall Swindell, Product Manager, Team 33
Regulatory Management Branch I
Antimicrobials Division (7510C)

FROM: Srinivas Gowda, Microbiologist/Chemist Srinivas Gowda 1/22/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

THRU: Siroos Mostaghimi, Acting Team Leader, Team One NCook for 1/27/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

Norm Cook, Chief 1/27/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

DP Barcodes: D289027
Decision #: 220066
Case Type: New Registration
PC Codes: 119093
Chemical Name: 1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

EPA File Symbol: 43813-ET
MRID No.: 456739-08 & 456739-09
Data Submitter: Janssen Pharmaceutica Inc.
CAS#: 122454-29-9
Common Name: AC303268

INTRODUCTION:

Janssen Pharmaceutica Inc. has submitted the hydrolysis study for 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- (R107894 also known as CL 303268) to meet the U.S. Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide Assessment Guidelines, Subdivision N, § 161-1 in support of new registration of the product, ECONEA™ Technical, EPA File Symbol 43813-ET, for formulation of antifouling treatment products. The submitted hydrolysis study has undergone review by Srinivas Gowda of Antimicrobials Division's Risk Assessment and Science Support Branch.

BACKGROUND:

1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- is an active ingredient in ECONEA™ Technical Anti-fouling Preservative. R107894 is the same chemical as 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- (also known as AC303,268). The submitted study was conducted to determine the Hydrolytic stability of [^{14}C]-R107894 to support the registration of ECONEA™ Technical Anti-fouling Preservative, EPA File Symbol 4813-ET.

The Hydrolysis study entitled "Determination of the Hydrolytic Stability of [^{14}C]-R107894" by J.A. Mackie, Inveresk Research, Tranent, EH33 2NE, Scotland, Inveresk Report No.15348, Inveresk Project No. 390042, dated December 22, 1997, has been submitted to the Agency (MRID Number 456739-08) to fulfill the Hydrolysis data requirements for the active ingredient, 1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

Supplement to Hydrolytic Stability Report No. 15365, "Identification of Hydrolytic Degradation Products of [^{14}C]-R107894" by F.M. Milligan, S.G.P. Williams, and G.M. McGuire, Inveresk Research, Tranent. EH33 2NE, Scotland, Inveresk Report No. 15365, Inveresk Project No. 364871 dated December 17, 1997 (MRID Number 456739-09).

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The study was conducted in accordance with the requirements of the EPA Pesticide Assessment Guidelines, Subdivision N, Section 161-1 (October 1982) and aspects of the OECD Guideline 111 (1981).

COMPLIANCE: The study was performed in compliance with GLP standards as specified in 40 CFR Part 160. Signed and dated GLP, Quality Assurance, and Data Confidentiality Statements were provided.

A. MATERIALS:

1. Test Material [Phenyl-^{14}C(U)]-R107894

Chemical Structure: Refer to Attachment 1 for structures of R107894 with position of carbon-14 label.

Description: [Phenyl-^{14}C(U)]-R107894, also known as CL 303,268, was supplied by American Cyanamid, Princeton, USA. The test

material was supplied in ethanol as a liquid at a nominal concentration of 11 mg/mL.

Purity: Analytical purity: >99% Lot/Batch No.: 101-077-026
Radiochemical purity: >99% Lot/Batch No.: 101-077-026
Specific activity: 26.4 mCi/mmol, 75.4 µCi/mg
Locations of the label: Not stated

Stability: Product may decomposed at a rate of approximately 0.5% per month when stored at -20°C under argon.

2) Buffer Solution: Buffer solutions were made with Milli-Q water as follows:

Table 1: Description of buffer solutions.

pH	Type and final molarity of buffer	Composition
5	0.01M citric acid buffer	0.1M citric acid + 0.1M trisodium citrate The buffer solution was diluted to a final concentration of 0.01M using Milli-Q water and sterilized by filtration (0.2 µm filter).
7	0.01M TRIS maleic acid buffer	0.2M TRIS-maleic acid (TRIS + maleic acid) + 0.2M sodium hydroxide The buffer solution was diluted to a final concentration of 0.01 M using Milli-Q water and sterilized by filtration (0.2 µm filter).
9	0.01M borate buffer	0.025M sodium borate + 0.1M hydrochloric acid The buffer solution was diluted to a final concentration of 0.01 M using Milli-Q water and sterilized by filtration (0.2 µm filter).
Seawater	Synthetic seawater (non-buffered)	22 g/L NaCl 9.7 g/L $MgCl_2$ 3.7 g/L Na_2SO_4 (anhydrous) 1.0 g/L $CaCl_2$ (anhydrous) 0.65 g/L KCl 0.20 g/L $NaHCO_3$ 0.023 g/L H_3BO_3

B. EXPERIMENTAL CONDITIONS

1) Preliminary Study:

Testing was performed for adsorption [^{14}C]-R107894 to the glassware. [^{14}C]-R107894 in ethanol (10 µL) was dispensed into a volumetric flask, the ethanol was removed under a stream of nitrogen and [^{14}C]-R107894 was redissolved in acetonitrile (10 mL). This was then dispensed (1 mL) into glass jars, containing each of the test solutions (99 mL); the concentration of [^{14}C]-R107894 was approximately 25% of that which will be used in the study. The levels of radioactivity in these solutions were

determined immediately following the addition of [^{14}C]-R107894 and the following day. No adsorption to glass ware was observed.

2) Experimental conditions

Table 2: Experimental parameters

Parameters		**Details**
Duration of the study		30 days
Test concentrations (µg/g)		Nominal: 0.5 µg/g Measured: pH 5 solution - 0.47 µg/g pH 7 solution - 0.56 µg/g pH 9 solution - 0.50 µg/g Seawater - 0.56 µg/g
No. of replications		2
Preparation of test medium	volume used/treatment	250 ml
	method of sterilization	Autoclaving (1.03 x 10^5 Pa, approx. 20 minutes)
	co-solvent (type/concentration)	
Test apparatus (type/material/volume)		Each test solution was divided into two sterile amberlite jars (ca 250 ml) with Teflon-lined lids.
Details of traps for volatile, if any		
If no traps were used, is the test system closed/open		Closed
Is there any indication of the test material adsorbing to the walls of the test apparatus?		No (See Preliminary Study above)
Experimental conditions Temperature (°C) Lighting		The amberlite jars containing the test solutions were immediately placed in a water bath at the appropriate temperature (i.e., either 10 or 25 ± 1°C) and incubated in the dark.
Other details, if any		

3). Supplementary Experiments:

In a supplementary study, solutions of [^{14}C]-R107894 in aqueous buffer (pH 7 and pH 9) and seawater were incubated at 10°C and 25°C for up to 96 hours to investigate the hydrolytic stability of R107894. Two hydrolysis products were detected together with two unknowns (A and B) which were only present in the pH 7 samples. The hydrolysis products (CL 322,250 and CL 325,195) were confirmed as being present in all the samples analyzed and the unknowns were identified as isomers of a

condensation reaction between Tris(tris(hydroxymethyl)amino methane, from the pH 7 buffer) and CL 322,250. The unknowns were not true hydrolysis products from the incubation, but artifacts arising from the buffer used with the pH 7 samples.

4). Sampling:

Table 3: Sampling details.

Criteria	Details
Sampling intervals for the parent/transformation products	Each test solution was sampled at intervals of 0, 3, 6, 12, and 24 hours and at 2, 3, 4, 7 10, 14, 21, and 30 days after the test initiation.
Sampling method	For each test solution and temperature, duplicate samples of buffer (approx. 10 g) were transferred from the stock solution into glass vials, in a laminar flow cabinet. Aliquots of the sub-sample were taken for liquid scintillation counting.
Sampling methods for the volatile compounds, if any	N/A
Sampling intervals/times for: pH measurement	The pH of each replicate was measured using a pH meter immediately following each sampling.
Sample storage before analysis	The pH of the sub-samples was adjusted to approximately 3 (using pH paper) using 2 M hydrochloric acid to prevent further hydrolysis and was stored pending chromatographic analysis.
Other observation, if any (e.g.: precipitation, color change etc.)	As the study progressed, it became evident that the concentration of radioactivity in the pH 5 solution incubated at 10°C was declining because the parent compound precipitated out as the incubation progressed.

C. ANALYTICAL METHODS:

Radiolabled R107894 and the degradation products in the test solutions were characterized and quantified by HPLC and TLC. HPLC analysis was carried out using a Hewlett-Packard 1050 series HPLC equipped with an autosampler, UV detector (280 nm) and a solvent programmer, connected to an Intersil Phenyl guard and HPLC column (1 cm and 25 cm x 4.6 mm; 5 µm; Hichrom) and a Berthold LB 507A radioactivity monitor.

The following mobile phases and gradient were used at a flow rate of 1.0 mL/min:

Time (min)	% Acetonitrile	% 0.01 M sodium Citrate Buffer (pH 4)
0	5	95
60	95	5

Non-radiolabelled reference standards were dissolved in acetonitrile, mixed with Milli-Q water and injected into the HPLC column individually and as a mixture to determine standard retention times. Test solutions (including the pH 5/10°C buffer/acetonitrile sample from 30) were injected into the HPLC column directly and a mixture of reference standards were injected at regular intervals throughout the chromatographic analysis.

Aliquots of each sample were analyzed by TLC using a silica gel $60F_{254}$ TLC plate, developed in toluene:acetone:methanol:acetic acid (75:30:6:0.5, by volume). The solvent was allowed to develop to a height of 170 mm. Non-radiolabelled R107894, CL 322,250, and CL 325,195 were co-chromatographed with each sample. Following chromatography, quantification of radioactivity present on TLC plates was performed using a molecular Dynamics phosphor imager. Standards were visualized by irradiation with UV light (254 nm). Co-chromatography of standards with radioactivity was used for the tentative identification of degradation products.

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS:

Overall, the experimental conditions were maintained. The pH values ranged from 4.94 to 5.19, 6.93 to 7.06, 8.90 to 9.15, and 7.79 to 8.18 in each of the respective pH 5, 7, 9 and seawater solutions. The controlled water baths maintained an accuracy of ± 0.1°C.

B. MASS BALANCE:

Total radiocarbon recovery ranged from 61.7 to 102.1% of the applied amount at pH 5 (10°C), 95.7 to 104.3% of the applied amount at pH 5 (25°C), 85.7 to 91.1% of the applied amount at pH 7 (10°C), 87.5 to 91.1% of the applied amount at pH 7 (25°C), 100.0 to 104.0% of the applied amount at pH 9 (10°C), 102.0 to 106.0% of the applied amount at pH 9 (25°C), 85.7 to 87.5% of the applied amount in seawater (10°C), and 87.5 to 91.1% of the applied amount in seawater (25°C).

Table 4: Hydrolysis of R107894, HPLC results expressed as percentage of the applied radioactivity at pH 5 (10°C) (mean value of two replicate samples).

Compound		Sampling times												
		Hours					Days							
		0	3	6	12	24	2	3	4	7	10	14	21	30
Parent compound - R107894		94.0	91.9	91.8	92.7	91.6	91.1	92.6	89.9	91.7	90.6	88.7	85.3	80.9
CL 322,250		0.73	1.39	1.63	0.77	0.56	2.07	1.67	2.43	2.67	3.27	3.86	6.18	9.41
CL 325,195		1.41	1.94	2.10	1.30	2.20	2.26	1.8	3.22	2.68	2.53	2.64	2.87	4.20
Unknown C		2.15	2.50	2.55	3.10	3.02	2.21	2.25	2.12	0.85	1.83	2.35	2.43	3.03
Unknown D		1.71	2.34	1.98	2.18	2.63	2.37	1.74	2.36	2.12	1.80	1.86	2.62	2.49
Unknown G		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.61	0.61	ND
Unidentified radioactivity, if any														
Volatiles	CO_2													
	volatile organic 1 volatile organic n Total													
Total % recovery		100	100	100	100	100	100	100	100	100	100	100	100	100

Table 5: Hydrolysis of R107894, HPLC results expressed as percentage of the applied radioactivity at pH 5 (25°C) (mean value of two replicate samples).

Compound		Sampling times												
		Hours					Days							
		0	3	6	12	24	2	3	4	7	10	14	21	30
Parent compound - R107894		93.3	91.9	91.1	91.7	88.2	82.2	80.6	78.1	65.4	60.2	46.8	33.9	22.2
CL 322,250		0.59	2.01	2.55	3.29	6.07	11.6	14.3	17.1	29.8	35.4	49.0	62.2	73.9
CL 325,195		1.89	2.06	2.77	1.94	2.22	2.86	1.95	1.88	2.12	1.86	1.64	1.35	1.66
Unknown C		1.88	2.06	1.88	1.62	1.33	1.58	1.45	1.46	1.38	1.19	0.93	1.27	1.06
Unknown D		2.32	2.02	1.77	1.51	2.18	1.78	1.69	1.46	1.29	1.39	1.70	1.31	1.29
Unidentified radioactivity, if any														
Volatiles	CO_2													
	volatile organic 1 volatile organic n Total													
Total % recovery		100	100	100	100	100	100	100	100	100	100	100	100	100

Table 6: Hydrolysis of R107894, HPLC results expressed as percentage of the applied radioactivity at pH 7 (10°C) (mean value of two replicate samples).

Compound		Sampling times												
		Hours					Days							
		0	3	6	12	24	2	3	4	7	10	14	21	30
Parent compound - R107894		77.9	74.7	71.1	66.2	59.1	48.1	34.6	30.2	14.5	6.22	2.69	ND	ND
CL 322,250		12.0	14.8	18.5	21.7	26.2	33.6	44.4	48.7	61.7	66.9	70.2	72.7	71.6
CL 325,195		1.34	0.82	0.76	1.44	1.62	1.29	0.44	0.73	0.70	0.65	0.84	0.76	0.32
Unknown A		2.20	2.12	2.46	2.90	3.29	4.63	5.79	5.28	4.63	3.60	2.59	1.26	0.91
Unknown B		3.74	4.13	3.96	4.84	6.74	9.69	12.1	12.5	16.1	20.4	21.1	22.4	25.8
Unknown C		1.16	1.80	1.83	1.40	1.12	1.24	1.09	1.30	0.99	0.78	0.98	1.14	ND
Unknown D		1.78	1.64	1.47	1.61	1.93	1.47	1.63	1.31	1.36	1.46	1.62	1.70	1.40
Unidentified radioactivity, if any														
Volatiles	CO_2													
	volatile organic 1 volatile organic n Total													
Total % recovery		100	100	100	100	100	100	100	100	100	100	100	100	100

Table 7: Hydrolysis of R107894, HPLC results expressed as percentage of the applied radioactivity at pH 7 (25°C) (mean value of two replicate samples).

Compound		Sampling times												
		Hours					Days							
		0	3	6	12	24	2	3	4	7	10	14	21	30
Parent compound - R107894		78.4	57.9	45.1	27.7	9.78	1.48	ND	ND	ND	ND	ND	ND	ND
CL 322,250		11.5	27.2	35.9	47.6	59.6	63.5	69.5	70.3	72.4	69.4	68.1	72.0	67.5
CL 325,195		1.06	1.17	1.41	1.15	ND	0.84	0.74	ND	ND	0.41	0.34	ND	ND
Unknown A		2.30	4.14	5.17	6.92	7.18	3.93	1.70	1.97	1.29	1.52	1.80	1.72	1.66
Unknown B		4.05	6.97	9.55	13.7	20.1	27.9	26.8	26.4	25.3	27.5	28.3	24.9	29.6
Unknown C		1.45	1.17	1.10	1.38	0.86	0.46	ND	0.68	1.03	ND	ND	ND	ND
Unknown D		1.35	1.48	1.82	1.59	0.78	1.94	1.27	0.60	ND	1.25	1.48	1.39	1.23
Unidentified radioactivity, if any														
Volatiles	CO_2													
	volatile organic 1 volatile organic n Total													
Total % recovery		100	100	100	100	98	100	100	100	100	100	100	100	100

Table 8: Hydrolysis of R107894, HPLC results expressed as percentage of the applied radioactivity at pH 9 (10°C) (mean value of two replicate samples).

Compound		Sampling times												
		Hours					Days							
		0	3	6	12	24	2	3	4	7	10	14	21	30
Parent compound - R107894		51.4	41.9	34.5	27.3	16.0	3.28	0.78	ND	ND	ND	ND	ND	ND
CL 322,250		44.3	52.9	60.4	67.9	79.2	90.7	94.4	94.7	95.0	94.1	94.5	95.6	96.2
CL 325,195		1.52	2.20	2.38	2.34	2.12	2.32	2.05	1.88	2.34	2.48	2.69	ND	ND
Unknown A		ND	ND	0.32	ND	ND	1.14	0.47	1.03	0.72	1.43	1.03	1.04	0.79
Unknown B		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	2.00	1.72
Unknown C		1.22	1.17	0.84	1.27	1.23	1.36	0.75	1.21	0.39	0.33	0.36	ND	ND
Unknown D		1.56	1.83	1.55	1.31	1.51	1.25	1.58	1.20	1.54	1.66	1.45	1.34	1.33
Unidentified radioactivity, if any														
Volatiles	CO_2													
	volatile organic 1 volatile organic n Total													
Total % recovery		100	100	100	100	100	100	100	100	100	100	100	100	100

Table 9: Hydrolysis of R107894, HPLC results expressed as percentage of the applied radioactivity at pH 9 (25°C) (mean value of two replicate samples).

Compound		Sampling times												
		Hours					Days							
		0	3	6	12	24	2	3	4	7	10	14	21	30
Parent compound - R107894		52.3	21.5	8.77	1.78	ND	ND	ND	ND	ND	ND	ND	ND	ND
CL 322,250		43.4	73.8	86.7	94.2	96.0	95.6	95.2	95.9	96.9	95.6	94.3	95.2	95.8
CL 325,195		2.14	2.17	2.18	1.76	2.19	1.90	2.00	1.95	1.67	1.66	2.24	1.55	1.26
Unknown A		0.41	0.73	0.60	0.56	ND	0.96	1.24	0.59	0.33	0.79	0.41	ND	0.38
Unknown C		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.61	1.00	ND
Unknown D		1.79	1.88	1.74	1.75	1.81	1.53	1.57	1.57	1.10	1.10	1.48	1.37	1.21
Unknown F		ND	ND	ND	ND	ND	ND	ND	ND	ND	0.88	1.01	0.92	1.38
Unidentified radioactivity, if any														
Volatiles	CO_2													
	volatile organic 1 volatile organic n Total													
Total % recovery		100	100	100	100	100	100	100	100	100	100	100	100	100

Table 10: Hydrolysis of R107894, HPLC results expressed as percentage of the applied radioactivity in seawater (10°C) (mean value of two replicate samples).

Compound		Sampling times												
		Hours					Days							
		0	3	6	12	24	2	3	4	7	10	14	21	30
Parent compound - R107894		54.9	47.0	44.5	34.7	20.2	5.21	2.37	ND	ND	ND	ND	ND	ND
CL 322,250		39.3	47.8	51.0	60.4	74.8	90.2	91.6	95.7	94.3	95.0	95.2	95.8	95.5
CL 325,195		2.35	2.67	2.76	2.83	2.30	2.34	2.53	2.25	2.60	2.18	2.60	2.21	2.06
Unknown A		ND	ND	ND	ND	ND	ND	0.51	ND	0.79	0.78	0.40	0.59	1.27
Unknown C		1.62	1.15	0.53	1.16	1.15	1.26	1.67	0.61	0.83	0.57	ND	ND	ND
Unknown D		1.87	1.42	1.31	1.01	1.62	1.02	1.34	1.41	1.53	1.49	1.79	1.46	1.21
Unidentificd radioactivity, if any														
Volatiles	CO_2													
	volatile organic 1 volatile organic n Total													
Total % recovery		100	100	100	100	100	100	100	100	100	100	100	100	100

Table 11: Hydrolysis of R107894, HPLC results expressed as percentage of the applied radioactivity in seawater (25°C) (mean value of two replicate samples).

Compound		Sampling times												
		Hours					Days							
		0	3	6	12	24	2	3	4	7	10	14	21	30
Parent compound - R107894		58.0	24.4	12.9	2.17	ND	ND	ND	ND	ND	ND	ND	ND	ND
CL 322,250		37.3	70.2	82.2	93.4	96.3	95.6	95.1	95.6	95.5	94.9	94.3	94.8	95.2
CL 325,195		2.38	2.73	2.37	1.99	2.43	2.07	2.40	2.27	2.45	1.83	2.16	1.79	1.10
Unknown A		ND	0.36	ND	ND	ND	1.00	1.10	1.13	0.51	1.09	0.83	1.05	0.71
Unknown C		0.99	0.98	0.89	1.04	ND	ND	ND	ND	ND	ND	ND	ND	ND
Unknown D		1.36	1.35	1.63	1.37	1.29	1.36	1.46	1.04	1.56	1.31	1.41	1.15	1.25
Unknown F		ND	ND	ND	ND	ND	ND	ND	ND	ND	0.87	1.29	1.18	1.74
Unidentified radioactivity, if any														
Volatiles	CO_2													
	volatile organic 1 volatile organic n Total													
Total % recovery		100	100	100	100	100	100	100	100	100	100	100	100	100

C. TRANSFORMATION OF PARENT COMPOUND:

At test termination, the concentration of the parent compound at 10°C decreased from 94.0% at day 0 to 80.9% of the initial at pH 5, decreased from 77.9% of the initial at day 0 to not detectable by day 21 at pH 7, decreased from 51.4% of the initial at day 0 to not detectable by day 4 at pH 9, and decreased from 54.9% of the initial at day 0 to not detectable by day 4 in seawater. In the corresponding 25°C test conditions, the concentration of the parent compound decreased from 93.3% at day 0 to 22.2% of the initial at pH 5, decreased from 78.4% of the initial at day 0 to not detectable by day 3 at pH 7, decreased from 52.3% of the initial at day 0 to not detectable by 24 hours at pH 9, and decreased from 58.0% of the initial at day 0 to not detectable by 24 hours in seawater.

TRANSFORMATION PRODUCTS:

At pH 5 (10°C) there were no major transformation products detected. At pH 7, the major transformation products detected were CL 322,250 and Unknown B with maximum concentrations of 72.7% and 25.8% of the applied observed on the 21st and 30th days of incubation, respectively. At pH 9, the major transformation product detected was CL 322,250, with a maximum concentration of 96.2% of the applied amount observed on the 30th day of incubation. In seawater, the major transformation product detected was CL 322,250 with a maximum concentration of 95.8% of the applied amount observed on the 21st day of incubation. The minor transformation products detected at pH 5 were CL 322,250; CL 325,195; Unknown C; Unknown D; and Unknown G formed at maximum concentrations of 9.4, 4.2, 3.1, 2.6, and 0.61% of the applied, respectively. The minor transformation products detected at pH 7 were CL 325,195; Unknown A; Unknown C; and Unknown D formed at maximum concentrations of 1.6, 5.8, 1.8, and 1.9% of the applied, respectively. The minor transformation products detected at pH 9 were CL 325,195; Unknown A; Unknown B; Unknown C; and Unknown D formed at maximum concentrations of 2.7, 1.4, 2.0, 1.4, and 1.8% of the applied, respectively. The minor transformation products detected in seawater were CL 325,195; Unknown A; Unknown C; and Unknown D formed at maximum concentrations of 2.8, 1.3, 1.7, and 1.9% of the applied, respectively. Volatiles were not formed.

At pH 5 (25°C), the major transformation product detected was CL 322,250 with a maximum concentration of 73.9% of the applied amount observed at the day 30. At pH 7, the major transformation products detected were CL 322,250 and Unknown B with maximum concentrations of 72.4% and 29.6% of the applied observed on the 7th and 30th days of incubation, respectively. At pH 9, the major transformation product detected was CL 322,250, with a maximum concentration of 96.9% of the applied amount observed on the 7th day of incubation. In seawater, the major transformation product detected was CL 322,250 with a maximum concentration of 96.3% of the applied amount observed 24 hours after incubation. The minor transformation products detected at pH 5 were CL 325,195; Unknown C; and Unknown D formed at maximum concentrations of 2.9, 2.1, and 2.3% of the applied, respectively. The minor transformation products detected at pH 7 were CL 325,195; Unknown A; Unknown C; and Unknown D formed at maximum concentration of 1.4, 7.2, 1.5, and 1.9% of the applied, respectively. The minor transformation products detected at pH 9 were CL 325,195; Unknown A; Unknown C; Unknown D; and Unknown F formed at maximum concentrations of 2.2, 1.2, 1.0, 1,9, and 1.4% of the applied, respectively. The minor transformation products detected in seawater were CL 325,195; Unknown A; Unknown C; Unknown D; and Unknown F formed at maximum concentrations of 2.7, 1.1, 1.0, 1.6, and 1.7% of the applied, respectively. Volatiles were not formed.

PATHWAYS:

Refer to Attachment 1 (attached) for chemical structures of R107894 and hydrolysis products.

Table 12: Chemical names for the transformation products of R107894.

Applicant's Code Name	CAS Number	CAS and/or IUPAC Chemical Name(s)	Chemical formula	Molecular weight
CL 322,250	Unknown	P-Chlorophenylcyanobromo pyrolecarboxyl		325.548
CL 325,195	Unknown	Hydroxy ketone metabolite		245.644

HALF-LIFE:

The half-life(lives) of [^{14}C]-R107894 at different pH values were:

pH	First order half life			DT50 (unit)	DT90 (unit)
	half-life	Regression equation	R^2		
5 (10°C)	168 days		0.953		
5 (25°C)	15 days		0.999		
7 (10°C)	69 hours		0.999		
7 (25°C)	8 hours		1		
9 (10°C)	12 hours		0.998		
9 (25°C)	2 hours		1		
Seawater (10°C)	15 hours		0.997		
Seawater @ 25°C	3 hours		0.998		

D. SUPPLEMENTARY EXPERIMENT-RESULTS:

In the supplementary study, two hydrolysis products were detected together with two unknowns (A and B) which were only present in the pH 7 samples. The hydrolysis products (CL 322,250 and CL 325,195) were confirmed as being present in all the samples analyzed and the unknowns were identified as isomers of a condensation reaction between Tris(tris(hydroxymethyl)amino methane, from the pH 7 buffer) and CL 322,250. The unknowns were not true hydrolysis products from the incubation, but artifacts arising from the buffer used with the pH 7 samples.

SUMMARY OF DATA:

Hydrolysis of radiolabelled [^{14}C]-R107894 at a nominal concentration of 0.5 µg/g was studied. The test solutions were incubated in the dark at nominal temperatures of 10 or 25 ± 1°C for up to 30 days in 0.01 M citrate buffer (pH 5), 0.01 M TRIS-maleic acid buffer (pH 7), 0.01 M borate buffer (pH 9) and seawater. The experiment was conducted in accordance with the requirements of the EPA Pesticide Assessment Guidelines, Subdivision N, Section 161-1 (October 1982) and aspects of the OECD

Guideline 111 (1981). The Guidelines followed in this study are now a part of the Harmonized Guidelines (OPPTS 835.2130). Samples were analyzed at 0, 3, 5, 12, and 24 hours and at 2, 3, 4, 7, 10, 14, 21, and 30 days. Radioactivity was quantified by direct injection using a liquid scintillation analyzer (Packard Tri-carb 1600 TR) and identification of the transformation products was conducted using HPLC (Hewlett-Packard 1050 series HPLC and a Berthold LB 507A radioactivity monitor) and TLC (Molecular Dynamics phosphor imager).

The radioactive balance was 87.2 ± 11.8%, 88.6 ± 2.0%, 102.2 ± 1.0%, and 87.1 ± 0.8% of the applied at pH 5, pH 7, pH 9, and seawater at 10°C, respectively. At test termination, the concentration of the parent compound at 10°C decreased from 94.0% at day 0 to 80.9% of the initial at pH 5, decreased from 77.9% of the initial at day 0 to not detectable by day 21 at pH 7, decreased from 51.4% of the initial at day 0 to not detectable by day 4 at pH 9, and decreased from 54.9% of the initial at day 0 to not detectable by day 4 in seawater. At pH 5 (10°C) there were no major transformation products detected. At pH 7 (10°C), the major transformation products detected were CL 322,250 and Unknown B with maximum concentrations of 72.7% and 25.8% of the applied observed on the 21st and 30th days of incubation, respectively. At pH 9, the major transformation product detected was CL 322,250, with a maximum concentration of 96.2% of the applied amount observed on the 30th day of incubation. In seawater, the major transformation product detected was CL 322,250 with a maximum concentration of 95.8% of the applied amount observed on the 21st day of incubation. The minor transformation products detected at pH 5 were CL 322,250; CL 325,195; Unknown C; Unknown D; and Unknown G formed at maximum concentrations of 9.4, 4.2, 3.1, 2.6, and 0.61% of the applied, respectively. The minor transformation products detected at pH 7 were CL 325,195; Unknown A; Unknown C; and Unknown D formed at maximum concentrations of 1.6, 5.8, 1.8, and 1.9% of the applied, respectively. The minor transformation products detected at pH 9 were CL 325,195; Unknown A; Unknown B; Unknown C; and Unknown D formed at maximum concentrations of 2.7, 1.4, 2.0, 1.4, and 1.8% of the applied, respectively. The minor transformation products detected in seawater were CL 325,195; Unknown A; Unknown C; and Unknown D formed at maximum concentrations of 2.8, 1.3, 1.7, and 1.9% of the applied, respectively. Volatiles were not formed.

The radioactive balance was 100.7 ± 2.2%, 89.6 ± 1.4%, 102.6 ± 1.3%, and 89.0 ± 1.2% of the applied at pH 5, pH 7, pH 9, and seawater at 25°C, respectively. At test termination, the concentration of the parent compound at 25°C decreased from 93.3% at day 0 to 22.2% of the initial at pH 5, decreased from 78.4% of the initial at day 0 to not detectable by day 3 at pH 7, decreased from 52.3% of the initial at day 0 to not detectable by 24 hours at pH 9, and decreased from 58.0% of the initial at day 0 to not detectable by 24 hours in seawater. At pH 5, the major transformation product detected was CL 322,250 with a maximum concentration of 73.9% of the applied amount observed at the day 30. At pH 7, the major transformation products detected were CL 322,250 and Unknown B with maximum concentrations of 72.4% and 29.6% of the applied observed on the 7th and 30th days of incubation, respectively. At pH 9, the major transformation product detected was CL 322,250, with a maximum concentration of 96.9% of the applied amount observed on the 7th day of incubation. In seawater, the major transformation product detected was CL 322,250 with a maximum concentration of 96.3% of the applied amount observed 24 hours after incubation. The minor transformation products detected at pH 5 were CL 325,195; Unknown C; and Unknown D formed at maximum concentrations of 2.9, 2.1, and 2.3% of the applied, respectively. The minor transformation products detected at pH 7 were CL 325,195; Unknown A; Unknown C; and Unknown D formed at maximum concentration of 1.4, 7.2, 1.5, and 1.9% of the applied, respectively. The minor transformation products detected at pH 9 were CL 325,195; Unknown A; Unknown C; Unknown D; and Unknown F formed at maximum concentrations of 2.2, 1.2, 1.0, 1,9, and 1.4% of the applied, respectively. The minor transformation products detected in seawater were CL 325,195; Unknown A; Unknown C; Unknown D; and Unknown F formed at maximum concentrations of 2.7, 1.1, 1.0, 1.6, and 1.7% of the applied, respectively. Volatiles were not formed.

The hydrolytic half-lives of [^{14}C]-R107894 in pH 5, pH 7, pH 9 and seawater at 25°C were calculated as 15 days, and 8, 2, and 3 hours, respectively. The corresponding values for [^{14}C]-R107894 incubated at 10°C were 168 days, and 69, 12, and 15 hours, respectively. [^{14}C]-R107894 was found to be hydrolytically unstable under the conditions of the test. Rapid hydrolysis was observed in pH 7, pH 9, and seawater incubated at 25°C, in comparison with that observed at pH 5. While hydrolysis was slower at 10°C, [^{14}C]-R107894 would still be classified as unstable.

In a supplementary study, solutions of [^{14}C]-R107894 in aqueous buffer (pH 7 and pH 9) and seawater were incubated at 10°C and 25°C for up to 96 hours to investigate the hydrolytic stability of R107894. Two hydrolysis products were detected together with two unknowns (A and B) which were only present in the pH 7 samples. The hydrolysis products (CL 322,250 and CL 325,195) were confirmed as being present in all the samples analyzed and the unknowns were identified as isomers of a condensation reaction between Tris(tris(hydroxymethyl)amino methane, from the pH 7 buffer) and CL 322,250. The unknowns were not true hydrolysis products from the incubation, but artifacts arising from the buffer used with the pH 7 samples.

This study is classified acceptable and satisfies the guideline requirement for an hydrolysis study.

RESULTS SYNOPSIS:

Test	Half-life	Major transformation products
pH 5 @ 10°C	168 days	No major transformation products, only minor transformation products
pH 5 @ 25°C	15 days	CL 322,250
pH 7 @ 10°C	69 hours	CL 322,250 and Unknown B
pH 7 @ 25°C	8 hours	CL 322,250 and Unknown B
pH 9 @ 10°C	12 hours	CL 322,250
pH 9 @ 25°C	2 hours	CL 322,250
Seawater @ 10°C	15 hours	CL 322,250
Seawater @ 25°C	3 hours	CL 322,250

RASSB's CONCLUSIONS AND RECOMMENDATIONS:

Risk Assessment and Science Support Branch (RASSB) concludes that the submitted hydrolysis data developed by the U.S. Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide Assessment Guidelines, Subdivision N, § 161-1 and OECD Guideline 111 on R107894 (CL 303,268) satisfies the EPA's Hydrolysis data requirements and the findings/conclusions are scientifically sound.

^{14}C-R107894 was rapidly hydrolyzed primarily to CL322,250 and traces of CL 325,195. Half lives were 15 days, 8 hours, 2 hours, and 3 hours at pH5, pH7, pH9 and in seawater at 25°C. Half lives were 168 days, 69 hours, 12 hours and 15 hours at pH5, pH7, pH9 and seawater at 10°C.

RASSB recommends that the submitted hydrolysis study under the MRID Nos. 456739-08 and 456739-09 be accepted to satisfy the EPA's Hydrolysis data requirements for the active ingredient, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- (also known as AC 303268) .

cc: Srinivas Gowda/RASSB/AD

Chemical (119093)AD

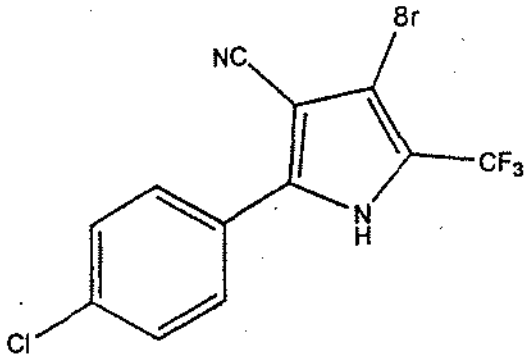
ATTACHMENTS:

1. Structure of [^{14}C]-R107894 and Hydrolysis Products

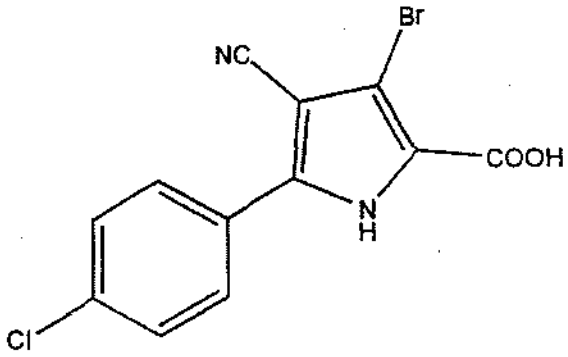
ATTACHMENT 1

Structure of R107894 and Putative Hydrolysis Products

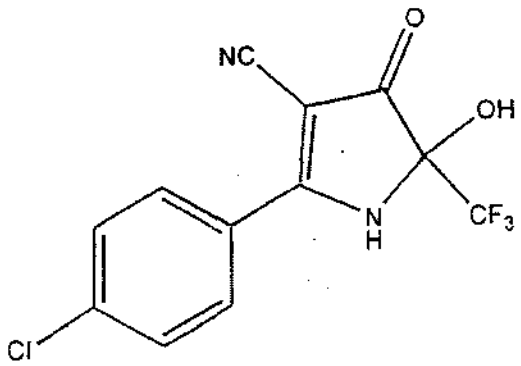
R107894



CL 322,250



CL 325,195



DP #: (289027) Decision #: 220066

DATA PACKAGE BEAN SHEET

Date: 27-Jan-2004

* * * Registration Information * * *

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA

Risk Manager: RM 33 - Marshall Swindell - (703) 308-6341 Room# CM-2 308H

Risk Manager Reviewer: Karen Leavy KLEAVY

Sent Date: 19-Mar-2003 Calculated Due Date: 18-Sep-2003 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (115) NEW INGREDIENT;NEW REGISTRATION;NON-FOOD/FEED USE;

Ingredients: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-(99%)

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 20-Mar-2003 Due Back:

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title:

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

	Assigned To	Date In	Date Out	
Organization:	AD / RASSB	20-Mar-2003	27-Jan-2004	Administrative Due Date: 18-Jul-2003
Team Name:	RASSB1	03-Apr-2003	27-Jan-2004	Negotiated Due Date:
Reviewer Name:	Gowda, Srinivas	03-Apr-2003	22-Jan-2004	Projected Completion Date:
Contractor Name:				

* * * Studies Sent for Review * * *

No Studies

* * * Additional Data Package for this Decision * * *

Printed on Page 3

* * * Data Package Instructions * * *

Please review new chemical fate/leaching data foracceptability.
(SMOSTAGH)

DP#: (289027) *** Additional Data Package for this Decision *** Decision#: (220066)

DP #	Division/Branch	Date Sent	Date Due	Instructions?	CSF	label
289021	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289021	AD / RMB1	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289026	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289026	AD / RMB1	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289029	AD / RMB1	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289029	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289031	AD / RMB1	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289031	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289033	AD / RMB1	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289033	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
290345	AD / RMB1	27-Jan-2004	27-Jan-2004	○ Yes ○ No	○ Yes ● No	○ Yes ● No
290345	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	○ Yes ● No	○ Yes ● No
292015	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
292015	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	● Yes ○ No	● Yes ○ No
295928	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	○ Yes ● No	○ Yes ● No
295928	AD / RASSB	27-Jan-2004	27-Jan-2004	○ Yes ○ No	○ Yes ● No	○ Yes ● No

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 22, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Review of Anaerobic Degradation Study for ECONEA™ Technical Containing AC 303268 Antifoulant

TO: Marshall Swindell, Product Manager, Team 33
Regulatory Management Branch 1
Antimicrobials Division (7510C)

FROM: Srinivas Gowda, Microbiologist/Chemist Srinivas Gowda 1/22/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

THRU: Siroos Mostaghimi, Acting Team Leader, Team One 4/28/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

Norm Cook, Chief 1/28/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

DP Barcodes: D289027
Decision #: 220066
Case Type: New Registration
PC Codes: 119093
Chemical Name: 1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

EPA File Symbol: 43813-ET
MRID No.: 456739-10
Data Submitter: Janssen Pharmaceutica Inc.
CAS#: 122454-29-9
Common Name: AC303268

INTRODUCTION:

Janssen Pharmaceutica Inc. has submitted the anaerobic degradation study for the active ingredient, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- (also known as AC 303268) to meet the U.S. Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide Assessment Guidelines, Subdivision N, § 162-3 in support of new registration of ECONEA™ Technical, EPA File Symbol 43813-ET, for formulation of antifouling treatment products. The submitted anaerobic degradation study has undergone review by Srinivas Gowda of Antimicrobials Division's Risk Assessment and Science Support Branch.

BACKGROUND:

1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- is an new active ingredient in ECONEA™ Technical Anti-fouling Preservative. It is also known as AC303268.

CONCLUSIONS:

1a. AC 303268 was hydrolyzed to CL 322,250 and CL 325,195 in fresh and marine systems. DT_{50} was 10 days for freshwater and, 0.03 days for marine; DT_{90} was ~113 for freshwater and 0.83 days for marine.

2a. Major transformation products in fresh water and marine system: CL 322, 250 & CL 325, 195
2b. Minor transformation products: Seven unknown transformation products (A-G)

RECOMMENDATIONS:

This study is classified as acceptable and satisfies the guideline requirement for anaerobic degradation study in two water-sediment systems. RASSB recommends that the anaerobic degradation study for AC 303268 be accepted in support of registration of ECONEA™ Technical MUP registration.

ANAEROBIC BIOTRANSFORMATION OF [^{14}C]-R107894 IN TWO WATER/SEDIMENT SYSTEMS

DATA EVALUATION REPORT

PRODUCT FORMULATION: ECONEA™ Technical Anti-fouling Preservative

ACTIVE INGREDIENT: 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl), also known as AC 303268

BACKGROUND: The study was submitted to evaluate the anaerobic degradation of the active ingredient AC 303268 in two freshwater and two marine sediments. The study was conducted according to the Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide Assessment Guidelines, Subdivision N, § 162-3.

CITATION:

Author:	J.A. Mackie
Report Date:	January 12, 2000
Study Date:	Initiated on May 22, 1998 and completed on July 29, 1999
Study Title:	"The Anaerobic Degradation of [^{14}C]-R107894 in Two Water/Sediment Systems"
Laboratory Name:	Inveresk Research Tranent EH33 2NE Scotland
Laboratory Report No.:	17832
Sponsor:	Janssen Pharmaceutica N.V. Turnhoutseweg 30 B-2340 Beerse Belgium

OPPTS GUIDELINE NO.: Subdivision N, 162-3

EXECUTIVE SUMMARY:

The anaerobic biotransformation of [^{14}C]-R107894 was studied in both a freshwater-sediment and a marine-sediment test system from Scotland for 52 weeks in the dark at 21°C. [^{14}C]-R107894 was applied at the rate of 69 μg/L to the surface of the water in each sample. The sediment/water ratio used was 15g/150mL. The experiment was conducted in accordance with the EPA Pesticide Assessment Guidelines, Subdivision N, Paragraph 162-3, and in compliance with the 40 CFR Part 160 GLP standards. The test system consisted of borosilicate glass cylinders attached with traps for the collection of CO_2 and volatile organic compounds. Samples were analysed at 0, 3, 7, 14 and 30 days and 8, 13, 17, 26, 39, and 52 weeks of incubation. Surface water was separated from the sediment by decanting and transferred into separate amberlite jars. The water samples were not extracted and the sediment samples were extracted with acetonitrile twice with approximately 50 mL. [^{14}C]-R107894 residues were analysed by TLC (using a silica gel 60F_{254} TLC plate and developed in toluene:acetone:methanol:acetic acid) and HPLC (using a Hewlett-Packard 1050 series). Identification of the transformation products was done by co-chromatography.

The test conditions outlined in the study protocol were maintained throughout the study. The mean total recovery of radiolabelled material after 52 weeks was 100.4±4.8% and 96.97±2.2% of the applied in the freshwater-sediment system and the marine-sediment system, respectively. The mean total recovery of radiolabelled material in the surface water and sediment of the freshwater test system was 26.30±1.1% and 22.91±0.9% of the applied amount, respectively. In the marine test system, the mean total recovery of radiolabelled material in the surface water and sediment was 57.68±0.2% and 22.46±1.2% of the applied amount, respectively.

In the fresh water test system, extractable [^{14}C]-residues in sediment decreased from a high of 62.80% at day 7 to 22.91% of the applied amount at the end of incubation period. Non-extractable [^{14}C]-residues in sediment increased from a low of 0.30% at day 3 to 50.96% of the applied amount at the end of the incubation period. In the marine test system, extractable [^{14}C]-residues in sediment decreased from a high of 32.29% at day 14 to 22.46% of the applied amount at the end of incubation period. Non-extractable [^{14}C]-residues in sediment increased from a low of 1.01% at day 3 to 16.52% of the applied amount at the end of incubation period. At the end of the study, 0.11% and 0.02% of the recovered radioactivity was

present as CO_2 and volatile organic compounds, respectively, in the marine test system. In the fresh water test system, 0.04% and 0.02% of the recovered radioactivity was present as CO_2 and volatile organic compounds, respectively.

In the fresh water test system, the concentration of R107894 in surface water and sediment decreased from 90.19% at day 0 to 1.80% of the applied amount at study termination. In the marine test system, the concentration of R107894 in surface water and sediment decreased from 92.36% to 0.06% of the applied amount at study termination.

The major transformation products of both the fresh water system and the marine system detected by HPLC analysis in water and sediment were CL 322,250 and CL 325,195. Maximum and minimum concentrations in the water of the freshwater test system were 44.10% and 2.56% of the applied amount, for CL 322,250, while CL 325,195 was reported to be below the detection limit throughout the incubation period. Maximum and minimum concentrations in the water of the marine test system were 60.34% and 1.99% of the applied amount for CL 322,250, and 6.64% and below the detection limit for CL 325,195. Maximum and minimum concentrations in the sediment of the freshwater test system were 10.05% and 4.62% of the applied amount for CL 322,250, and 1.29% and 1.16% of the applied amount for CL 325,195. Maximum and minimum concentrations in the sediment of the marine test system were 16.35% and 2.38% of the applied amount, for CL 322,250, and 1.39% and 0.52% of the applied amount for CL 325,195.

According to the Registrant, the 1st order 50% decline time (DT50) for the freshwater test system was 10 days and the 90% decline time (DT90) was 113 days. For the marine test system, the 1.5 order DT50 was 0.03 days and the DT90 was 0.83 days. The rates of degradation were estimated by fitting the data to the Timmes, Frelise, and Laska model (validated by Bayer AG). The authors noted that degradation was very rapid in the marine test system and that the degradation rates of R107894 in each of the compartments could not be estimated with any degree of accuracy due to the variability in the total levels of radioactivity in each of the compartments over the incubation period. RASSB was unable to calculate a half-life for the marine test system (including water and sediment compartments and the entire system) as well as the water compartment of the fresh-water system because several values were reported as non-detect and a detection limit was not provided. RASSB calculated half-lives for the sediment compartment and for the entire fresh-water system based on a first order regression of percent of dose values. These half-lives were much higher than those reported in the study report, which could not be verified. However, the differences may be because the Registrant used a model to calculate their values, while RASSB used a regression analysis.

Results Synopsis:

Test system used: Fresh-water and marine water/sediment test systems

	Registrant	RASSB
Fresh-water system		
DT50 in water:	Not provided	Could not be calculated[a]
Half-life/DT50 in sediment:	Not provided	71 days
Half-life/DT50 in the entire system:	10 days	63 days
Marine system		
DT50 in water:	Not provided	Could not be calculated
Half-life/DT50 in sediment:	Not provided	Could not be calculated
Half-life/DT50 in the entire system:	0.03 days	Could not be calculated

Major transformation products: CL 322, 250
CL 325, 195
Minor transformation products: Seven unknown transformation products (A-G)

[a] Several values reported as non-detect; no detection limit provided

Study Acceptability: This study is classified as acceptable and satisfies the guideline requirement for anaerobic biotransformation study in water-sediment system. However, more detailed information should be provided for the Timme, Frehse, and Laska model, and in addition, the Registrant should specify which data were used to calculate the DT50 and DT90 values before full acceptance of the study.

I. MATERIALS AND METHODS

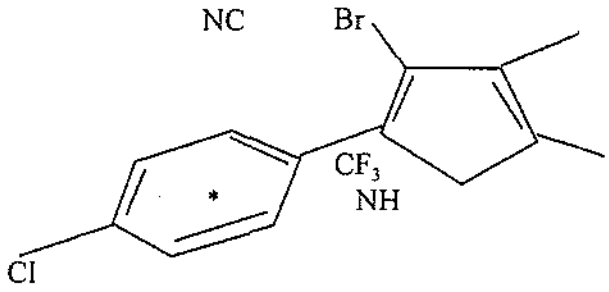
GUIDELINE FOLLOWED: EPA Pesticide Assessment Guidelines, Subdivision N, 162-3

COMPLIANCE: Signed and dated statement of GLP compliance as specified in 40 CFR Part 160 included with report. Report also included signed and dated Data Confidentiality and Quality Assurance statements.

A. MATERIALS:

1. Test Material [Phenyl-^{14}C(U)]-R107894

Chemical Structure:



* Position of Carbon-14 Label

Description: Technical

Purity:

Radiolabelled Lot/Batch No.:	101-077-026.
Analytical purity:	>99% on 6/8/96
Radiochemical purity:	As stated on specification sheet: >99% on 6/8/96 As determined by TLC and HPLC under Iveresk Project Number 390770 (mean radiochemical purity): 97.37%
Specific activity:	26.4 mCi/mmol, 75.4 μCi/mg
Locations of the label:	Radiolabel is located within the phenol ring.

Non-radiolabelled R107894 Lot/Batch No.:	AC6943-127
CL 322,250 Lot/Batch No.:	AC9014-97A
CL 325,195 Lot/Batch No.:	AC9014-93B

Storage conditions of test chemicals: The test material was supplied in ethanol. The storage conditions in the laboratory were not provided.

Physico-chemical properties of test material: See Table 1.

Table 1. Physico-chemical properties of R107894

Parameter	Values	Comments
Water solubility	Not provided	–
Vapor pressure/volatility	Not provided	–
UV absorption	Not provided	–
pK_a	Not provided	–
K_{ow}/log K_{ow}	Not provided	–
Stability of Compound at room temperature	Study report states that the exact rate of decomposition is unknown.	–

2. Water-sediment collection, storage and properties

Table 2. Description of water collection and storage

Description	Details
Geographic location	Fresh water: collected from wetlands in Bogton Loch Salt water: supplied from Flotta laboratory supply; pumped from Scapa Flow
Pesticide use history at the collection site	Fresh: agrochemical free catchment Marine: Not provided.
Collection procedures for water & sediment:	Not Provided
Sampling depth for water & sediment:	Fresh water: 54 cm Marine water: Not provided. Fresh sediment: 0-30 mm of loch sediment. Marine sediment: Not provided. *Depth of marine water adjacent to the sediment was 10cm.
Storage conditions	Fresh: samples stored at 4°C in the dark under aerobic conditions prior to delivery. Marine: 12 kg of sediment packed in 1 cool box for delivery. 40 liters of water packed in two 30 liter barrels for delivery.
Storage length	Fresh water/sediment samples collected on June 1st and received by the laboratory on June 5th. Salt water/sediment samples were collected on June 9th and received by the laboratory on June 15th. Samples were stored at 4°C prior to use in the experiments. Storage length was not provided.
Preparation of water and sediment samples (eg: water - filtered/not filtered; sediment - sieved/not sieved)	Fresh water: 20 liters of loch water filtered through a 0.2 mm sieve prior to supply Marine water: Pumped from Scapa Flow and passed through a 171 μm mesh. Fresh sediment: 12 kg of loch sediment collected and passed through a 2 mm sieve prior to delivery. Marine sediment: collected from Seaby Bay, returned to Flotta and sieved through a 600 μm mesh to remove Corophium.

Table 3. Properties of the water

Property	Ponds			
	Fresh		Marine	
Temperature (°C)	13.5		10	
pH	6.5		8.04	
Redox potential (mv)	Initial	Final	Initial	Final
	RepA: -9 RepB: -8	RepA: -174 RepB: -148	RepA: -3 RepB: -8	RepA: -143 RepB: -160
Oxygen concentration (mg/L)	98% (under surface of sediment) 96% (5 cm above sediment)		106%	
Dissolved organic carbon (%)	13.4		174.3	
Hardness (mg $CaCO_3$/L)	39		7100	
Electrical conductivity	NP		NP	
Biomass (mg microbial C/100 g or CFU or other)	NP		NP	

NP - not provided in the study report.

Table 4. Properties of the sediment

Property	Ponds			
	Fresh		Marine	
Textural classification	silt loam		loamy sand	
% sand	22.07		83.28	
% silt	55.92		13.75	
% clay	22.01		2.97	
pH	5.8 (in water)		7.7 (in water)	
Organic carbon (%)	2.5		0.8	
CEC (meq/100 g)	18.3		5.2	
Redox potential (mv)	Initial	Final	Initial	Final
	NP	NP	NP	NP
Bulk density (g/cm^3)	NP		NP	
Biomass (mg microbial C/100 g or CFU or other)	Initial	Final	Initial	Final
	NP	NP	NP	NP

NP - not provided in the study report.

B. EXPERIMENTAL DESIGN:

1. Preliminary experiments: No preliminary experiments reported.

2. Experimental conditions: See Table 5.

Table 5. Study design

Parameter	Details
Duration of the test	52 weeks
Water: Filtered/unfiltered water: Type and size of filter used, if any:	Filter water used for both fresh and marine systems. Fresh water filtered through a 2 mm sieve and salt water filtered through a 171 μm sieve.
Amount of sediment and water/ treatment	15 g of sediment per treatment 150 mL water per treatment
Water/sediment ratio	15 g:150 mL
Application rates (μg/μL)	69
Control conditions, if used (present differences from other treatments, i.e., sterile/non-sterile, experimental conditions)	Stability control samples were prepared by dispensing radiolabelled test solution directly into acetonitrile, the proposed extractant. Non-radiolabelled R107894 was administered to each of the control incubation units.
No. of replications	22 samples; 2 replicates per sampling time. Stability control samples prepared but not analyzed.
Test apparatus Type/material/volume Details of traps for CO_2 and organic volatile, if any	Samples of sediment placed into individual borosilicate glass cylinders (previously silanised; 15.9 cm^2 cross sectional area). First trap = safety trap; second trap = non-specific ^{14}C-organic volatiles; third trap = liberated $^{14}CO_2$
If no traps were used, is the system closed	N/A
Identity and concentration of co-solvent	Not provided
Pesticide application method Volume of the test solution used/treatment: Application method (eg: mixed/not mixed)	Not provided
Any indication of the test material adsorbing to the walls of the test apparatus	No adsorption to glassware was observed for any of the glass vessels.

Parameter		Details			
Microbial biomass/microbial population of the freshwater test system (sediment)		Pre-dose		Final	
	Rep	Bacteria	Spores	Bacteria	Spores
	A	80000	35000	29000	8300
	B	120000	37000	37000	11000
Microbial biomass/microbial population of the freshwater test system (water)		Pre-dose		Final	
	Rep	Bacteria	Spores	Bacteria	Spores
	A	249	15	31	1
	B	20	0	3	0
Microbial biomass/microbial population of the marine test system (sediment)		Pre-dose		Final	
	Rep	Bacteria	Spores	Bacteria	Spores
	A	35000	15000	46000	28000
	B	72000	34000	3900	20000
Microbial biomass/microbial population of the marine test system (water)		Pre-dose		Final	
	Rep	Bacteria	Spores	Bacteria	Spores
	A	270	90	110	1
	B	250	310	36	113
Experimental conditions:	Temperature (°C):	21			
	Continuous darkness (Yes/No)	Yes			
Other details, if any					

3. Anaerobic conditions: The test system was exposed to a moist stream of nitrogen via a dip tube extending to just below the water surface. Samples were measured at each sampling interval to determine the redox potential and oxygen concentration of the surface water.

4. Supplementary experiments: No supplementary experiments were mentioned in the study report.

5. Sampling: See Table 6.

Table 6. Sampling details

Criteria	Details
Sampling intervals	Duplicate incubation from each sediment type were measured at zero time (immediately following application), 3, 7, 14, and 30 days, and 8, 13, 17, 26, 39, and 52 weeks
Sampling method	The study report stated that traps were sampled and replenished at regular intervals throughout the incubation period. No specifics on sampling were provided.
Method of collection of CO_2 and organic volatile compounds	Gas mixture passed through a series of 3 traps. 1st: safety trap; 2nd: contained ethanediol to trap non-specific ^{14}C-organic volatiles; 3rd: contained ethanolamine to trap liberated $^{14}CO_2$; polyurethane plugs placed in neck and in safety trap to trap non-specific ^{14}C-organic volatiles
Sampling intervals/times for: sterility check, if sterile controls are used: redox potential:	At each sampling interval (0, 3, 7, 14, 30 days and 8, 13, 17, 26, 39, and 52 weeks), redox potential was sampled.
Sample storage before analysis	Details on storage of the samples before analysis was not provided.
Other observations, if any	

C. ANALYTICAL METHODS:

1. Separation of sediment and water:
Surface water was separated from sediment by careful decanting and then transfer into separate amberlite jars.

2. Extraction/clean up/concentration methods for water and sediment samples:

Water: After decanting, aliquots of the surface water were submitted for liquid scintillation counting. The remaining sample was acidified to approximately pH 3 using 2 M hydrochloric acid and then stored until analysis.

Sediment: Each sediment sample was extracted with acetonitrile by shaking for approximately 1 hour using an end-over-end shaker. The extract was then separated from the residue by centrifugation at 1000 rpm for 15 minutes. The amount of radioactivity in the supernatant was then determined by liquid scintillation counting. Residues were subjected to combustion analysis to quantify residual radioactive content.

3. Total ^{14}C measurement:
Total [^{14}C] was reported to be the summation of the total extractable [^{14}C]-activity (surface water and sediments), total $^{14}CO_2$, total volatile [^{14}C]-activity, total [^{14}C]-non-extractable residues, and

total [^{14}C]-activity found in the apparatus wash. The analysis methods for total sediment extractable and total non-extractable residues were provided above. Aliquots of surface waters, extracts, apparatus washes, and ethanediol and ethanolamine trap contents were added directly to the scintillant and counted by liquid scintillation counting. All radioassays were performed in duplicate.

Radioactivity was quantified using a liquid scintillation analyser (Packard Tri-Carb 1600TR) with automatic quench correction by external standard-channels ratio. Each individual sample was counted for 5 minutes.

4. Identification and quantification of parent and transformation products:
Radiolabelled R107894 and its degradation products in both sediment and water samples were characterized and quantified by HPLC and TLC. HPLC analysis was carried out using a Hewlett-Packard 1050 series HPLC equipped with an autosampler, UV detector and a solvent programer connected to an Inertsil Phenyl guard and HPLC column (1cm and 25cm x 4.6 mm; 5μm; Hirchrom) and either a Packard Flo-One A-100 Series radioactivity monitor, a Berthold LB 507A radioactivity monitor or a Gibson Model 202 fraction collector. Quantification of radioactivity ws performed by integrating the area under each peak or by submitting a fraction of the column eluate for liquid scintillation counting. Sample aliquots were submitted to TLC using a silica get 60F_{254} TLC plate and then developed in toluene:acetone:methanol:acetic acid (75:30:6:0.5, by volume). Non-radiolabelled R107894, CL 322,250 and CL 325,195 were chromatographed under each sample. Quantification of radioactivity present on TLC plates was then performed using a Molecular Dynamic phosphor imager.

5. Determination of non-extractable residues:
Following the extraction of the sediment samples, the residues were subjected to combustion analysis to quantify residual radioactive content. Triplicate portions of sediment residues, approximately 0.3 g each, were mixed with cellulose powder and 100 to 200 µL of Combustaid® before combusting in oxygen using a Packard Sample Oxidizer, Model 306. The combusted products were absorbed in Carbo-Sorb® mixed with Permafluor® V and the radioactivity was determined by liquid scintillation counting. A [^{14}C] standard was combusted at the beginning of each day and at regular intervals throughout the day to check combustion and trapping efficiencies.

6. Detection limits (LOD, LOQ) for the parent compound and transformation products:
The study report stated that a limit of reliable determination, for determination of radioactivity, of 30 d.p.m. above background count rate was instituted in their laboratory. A specific LOD or LOQ was not provided in the study report.

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS:
After application of the test solution, samples were incubated in the dark at a nominal temperature of 21°C for up to 52 weeks. The samples were connected to a continuous nitrogen gas flow system. Anaerobic conditions, temperature and other experimental conditions were maintained throughout the study.

B. MATERIAL BALANCE:
The mean total recovery of radiolabelled material after 52 weeks was 100.4 ± 4.8% and 96.97 ± 2.2 %

(mean ±std) of the applied amount in the freshwater-sediment system and the marine-sediment system, respectively (see Tables 7 and 8).

Table 7. Biotransformation of [^{14}C]-R107894, expressed as percentage of applied radioactivity (mean (s.d.)), in fresh water-sediment system under anaerobic conditions

Compound	Sampling times (days, hours, or other time period)										
	0	Day 3	Day 7	Day 14	Day 30	Week 8	Week 13	Week 17	Week 26	Week 39	Week 52
Surface water	60.77 (18.2)	39.59 (1.9)	25.56 (2.9)	44.10 (2.9)	21.97 (3.4)	17.13 (5.0)	10.51 (0.1)	15.48 (0.7)	15.57 (5.3)	23.20 (0.7)	26.31 (1.1)
Sediment extracts	35.63 (20.8)	54.35 (1.1)	62.81 (3.7)	34.79 (4.3)	50.16 (8.4)	41.19 (2.5)	28.67 (4.4)	26.94 (2.4)	22.87 (2.9)	20.12 (2.4)	22.91 (0.9)
$^{14}CO_2$	NS	0.03 (0)	0.01 (0)	0.02 (0)	0.03 (0)	0.03 (0)	0.03 (0)	0.04 (0)	0.05 (0.01)	0.05 (0.03)	0.04 (0)
^{14}C-volatiles	NS	ND	ND	ND	0.01 (0)	0.01 (0)	0.01 (0)	0.02 (0)	0.02 (0)	0.02 (0.01)	0.02 (0)
Non-extractable residues	2.43 (1.5)	0.34 (0.1)	7.67 (0.3)	24.97 (2.4)	24.73 (1.4)	35.57 (2.8)	52.51 (2.5)	54.69 (0.04)	60.79 (11.3)	55.50 (2.0)	50.96 (6.7)
Apparatus Wash	2.92 (3.2)	2.34 (1.1)	2.77 (3.4)	0.19 (0.1)	2.48 (1.7)	0.56 (0.4)	0.25 (0.2)	0.88 (1.0)	0.12 (0.02)	0.10 (0)	0.13 (0.01)
Total % recovery	101.7 (0.9)	96.64 (0.3)	98.81 (2.9)	104.1 (1.1)	99.37 (1.9)	94.48 (0.6)	91.97 (1.9)	98.04 (0.8)	99.40 (3.2)	98.98 (0.3)	100.4 (4.8)

NS - No sample
ND - Non-detect

Table 8. Biotransformation of [^{14}C]-R107894, expressed as percentage of applied radioactivity (mean (s.d.)), in marine-sediment system under anaerobic conditions

Compound	Sampling times (days, hours, or other time period)										
	0	0.167	0.375	Day 1	Day 30	Week 8	Week 14	Week 18	Week 20	Week 39	Week 52
Surface water	85.47 (0.6)	66.28 (3.6)	54.57 (1.9)	51.79 (2.1)	53.50 (0.7)	54.21 (2.9)	54.69 (0.8)	55.05 (0.05)	53.33 (0.2)	56.88 (0.4)	57.68 (0.2)
Sediment extracts	13.81 (1.3)	23.66 (1.2)	30.08 (0.1)	32.29 (0.1)	28.28 (0.1)	26.41 (1.1)	26.09 (0.02)	25.08 (0.7)	23.91 (0.5)	21.99 (1.3)	22.46 (1.2)
$^{14}CO_2$	NS	ND	ND	0.01 (0)	0.02 (0)	0.04 (0)	0.06 (0.01)	0.07 (0.02)	0.07 (0.01)	0.11 (0.02)	0.12 (0)
^{14}C-volatiles	NS	ND	ND	ND	0.01 (0)	0.01 (0)	ND	0.02 (0)	0.02 (0)	0.02 (0)	0.02 (0)
Non-extractable residues	4.35 (0.3)	1.82 (1.1)	8.41 (1.6)	11.81 (1.5)	13.23 (0.1)	13.61 (2.2)	12.87 (1.3)	13.31 (1.1)	16.88 (2.2)	17.94 (1.2)	16.52 (3.5)
Apparatus Wash	0.19 (0.1)	0.78 (0.7)	1.29 (1.0)	0.14 (0.03)	0.27 (0.1)	0.15 (0.01)	0.20 (0.03)	0.10 (0)	0.36 (0.3)	0.15 (0.1)	0.19 (0.1)
Total % recovery	103.8 (0.5)	92.53 (2.9)	94.35 (2.4)	96.03 (0.7)	95.31 (0.5)	94.42 (0.4)	93.9 (0.6)	93.61 (1.8)	94.56 (2.5)	97.08 (0.4)	96.97 (2.2)

NS - No sample
ND - Non-detect

C. TRANSFORMATION OF PARENT COMPOUND:

Fresh Water System:
According to HPLC analysis, the concentration of [^{14}C]-R107894 in water decreased from 57.63% of the applied amount at day 0 to below the detection limit at study termination. The concentration of [^{14}C]-R107894 in the sediment decreased from 32.56% at day 0 to 1.8% of the applied amount at the end of the study period.

Marine System:
According to HPLC analysis, the concentration of [^{14}C]-R107894 in water decreased from 82.48% of the applied amount at day 0 to below the detection limit at study termination. The concentration of [^{14}C]-R107894 in the sediment decreased from 9.88% at day 0 to 0.06% of the applied amount at the end of the study period.

The Registrant calculated a 50% decline time (DT50) and 90% decline time (DT90) of [^{14}C]-R107894 by fitting the data to the Timme, Frehse, and Laska model for both the anaerobic freshwater-sediment system and the marine-sediment system (see Table 9). The study report only provided DT50 and DT90 values for the entire system, because according to the Registrant degradation rates in each compartment could not be estimated due to the variability in the total levels of radioactivity in each of the compartments over the incubation period.

RASSB was not able to verify the values provided in the study report for either the fresh water system or the marine system. For the fresh water test system, RASSB was able to calculate half-lives, based on a

linear regression analysis of percent of dose values, for the sediment compartment and the entire system. These values were 70 days and 62 days for R107894 in the fresh water test system sediment and for the entire fresh water system, respectively. Values for the water compartment of the fresh water test system and for the entire marine test system, as well as its separate compartments, could not be calculated since several percent of dose values were reported as non-detect and a detection limit was not provided in the study report (see Table 9).

Table 9. Half-life/DT50 and DT90 Values for [^{14}C]-R107894

System	Model	DT50 (days)	DT90 (days)	Regression Equation	R
Registrant Calculated Values					
Fresh water	Square Root (1st Order)	10 days	113 days	NP[a]	NP
Marine	Square Root (1.5 Order)	0.03 days	0.83 days	NP	NP
RASSB Calculated Values					
Fresh water sediment entire	1st order regression	–[b] 71 days 63 days	– – –	– y = -0.0097x + 3.708 y = -0.0109x + 3.985	– 0.928 0.906
Marine water sediment entire	1st order regression	– – –	– – –	– – –	– – –

a Not provided
b Could not be calculated; no detection limit provided

TRANSFORMATION PRODUCTS:
The major transformation products of both the fresh water system and the marine system detected by HPLC analysis in water were CL 322,250 and CL 325,195. In the fresh water system, CL 322,250 was reported to have a maximum concentration of 44.10% of the applied amount, observed on day 14 of the incubation. The corresponding concentration of CL 322,250 in water at the end of the study period was 2.56% of the applied amount. CL 325,195 was reported to be below the detection limit in the water throughout the incubation period. In the marine system, CL 322,250 and CL 325,195 were reported to have maximum concentrations of 60.34% and 6.64% of the applied amount, respectively, observed on day 3 of the incubation. The corresponding concentration of CL 322,250 in water at the end of the study period was 1.99% of the applied amount, while the concentration of CL 325,195 was below the detection limit.

CL 322,250 and CL 325,195 were also the major transformation products detected in sediment in both the fresh water and marine test systems. According to the study report, maximum concentrations of CL 322,250 and CL 325,195 in the sediment of the fresh water system were 10.05% and 1.29% of the applied amount, observed on the 14th and 7th day of incubation, respectively. The corresponding concentrations in sediment at the end of the study period for the freshwater system were 4.62% and 1.16% of the applied amount, respectively. In the marine-sediment system, maximum concentrations in the sediment were reported to be 16.35% and 1.39% of the applied amount, observed on the 7th day and right after application (zero time), respectively. The corresponding concentrations in sediment of the

marine test system at the end of the study period were 2.38% and 0.52% of the applied amount, respectively.

Seven unknown transformation products (Unknowns A-G) were also identified and quantified. At the end of the study period, these compounds together accounted for 39.08% and 75.05% of the total applied amount, for the fresh water system and the marine system, respectively. Unknown compound B accounted for the highest percentage of all the unknowns (35.65% and 63.78% for the fresh water and marine test systems, respectively).

NON-EXTRACTABLE AND EXTRACTABLE RESIDUES:
In the fresh water test system, extractable [^{14}C]-residues in sediment decreased from a high of 62.80% at day 7 to 22.91% of the applied amount at the end of incubation period. Non-extractable [^{14}C]-residues in sediment increased from a low of 0.30% at day 3 to 50.96% of the applied amount at the end of incubation period. In the marine test system, extractable [^{14}C]-residues in sediment decreased from a high of 32.29% at day 14 to 22.46% of the applied amount at the end of incubation period. Non-extractable [^{14}C]-residues in sediment increased from a low of 1.01% at day 3 to 16.52% of the applied at the end of incubation period.

VOLATILIZATION:
At the end of the study, 0.11% and 0.02% of the recovered radioactivity was present as CO_2 and volatile organic compounds, respectively, in the marine test system. In the fresh water test system, 0.04% and 0.02% of the recovered radioactivity was present as CO_2 and volatile organic compounds, respectively.

TRANSFORMATION PATHWAY:
The transformation pathway was not provided in the study report.

D. SUPPLEMENTARY STUDY- RESULTS:
A supplementary study was not performed.

III. STUDY DEFICIENCIES:
The following study deficiencies were noted:

- The study report stated that controls were included in the study but the samples were not analyzed.
- A detection limit was not provided in the study report.

IV. REVIEWER'S COMMENTS:
The following issues of concern were noted:

- The raw data were not provided and therefore, the results presented could not be verified.
- The study report provided values for DT50 and DT90 but did not specify which data were used to calculate these values. It is assumed that these are decline times for the entire fresh water and marine test systems.
- RASSB was unable to verify the values provided in the study report for both the fresh water system or the marine system. For the fresh water test system, RASSB was able to calculate half-lives, based on a regression analysis of percent of dose values, for the sediment compartment and the entire system, however these values were much higher than those reported in the study report (71 days and

63 days for the fresh water test system sediment and for the entire fresh water system, respectively). The Registrant used the Timme, Frehse, and Laska model to determine the half lives and RASSB's determination was based on a linear regression analysis. Values for the water compartment of the fresh water test system and for the entire marine test system, as well as its separate compartments, could not be calculated since several percent of dose values were reported as non-detect and a detection limit was not provided in the study report.

- The Registrant should provided a more detailed presentation of (1) the Timme, Frehse, and Laska model and (2) what values were used to calculate the DT50 and the DT90.

V. REFERENCES:

No references were provided in the study report.

Conclusion: RASSB concludes that this missing information does not alter the acceptability of the study. The study is acceptable.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 22, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Review of Adsorption/Desorption Study for ECONEA™ Technical Containing AC 303268 Antifoulant

TO: Marshall Swindell, Product Manager, Team 33
Regulatory Management Branch I
Antimicrobials Division (7510C)

FROM: Srinivas Gowda, Microbiologist/Chemist Srinivas Gowda 1/22/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

THRU: Siroos Mostaghimi, Acting Team Leader, Team One 1/28/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

Norm Cook, Chief 1/28/04
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

DP Barcodes: D289027
Decision #: 220066
Case Type: New Registration
PC Codes: 119093
Chemical Name: 1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

EPA File Symbol: 43813-ET
MRID No.: 456739-13
Data Submitter: Janssen Pharmaceutica Inc.
CAS#: 122454-29-9
Common Name: AC303268

INTRODUCTION:

Janssen Pharmaceutica Inc. has submitted the Adsorption/Desorption Study for the active ingredient 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- (also known as AC 303,268) to meet the U.S. Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide Assessment Guidelines, Subdivision N, § 163-1 in support of new registration of ECONEA™ Technical, EPA File Symbol 43813-ET, for formulation of antifouling treatment products. The submitted adsorption/desorption study has undergone review by Srinivas Gowda of Antimicrobials Division's Risk Assessment and Science Support Branch.

BACKGROUND:

1H-Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)- is a new active ingredient in ECONEA™ Technical Anti-fouling Preservative. It is also known as AC303268.

CONCLUSIONS:

1a. K_f values were 446, 349, 22, and 183 in sandy loam, silt loam, sand, and loam soils, respectively.

1b. Average adsorption K_d values were 450, 335, 26, and 196 in sandy loam, silt loam, sand, and loam soils, respectively. The average adsorption K_{oc} values were 20440, 16733, 3582, and 5588 in sandy loam, silt loam, sand, and loam soils, respectively.

2a. Average desorption K_d values were 599, 568, 40, and 299 in sandy loam, silt loam, sand, and loam soils, respectively. The average desorption K_{oc} values were 27229, 28353, 5658, and 8543 for sandy loam, silt loam, sand, and loam soils, respectively. Desorption K_d and K_{oc} values were higher than those obtained for adsorption.

RECOMMENDATIONS:

This study is classified as acceptable and satisfies the guideline requirement for adsorption/desorption study in sediment. RASSB recommends that the Adsorption/Desorption Study for AC 303268 be accepted in support of ECONEA™ Technical MUP registration.

R107894 ADSORPTION/DESORPTION IN SEDIMENT

DATA EVALUATION REPORT

PRODUCT FORMULATION: ECONEA™ Technical Anti-Fouling Preservative

ACTIVE INGREDIENT: 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl), also known as AC 303268

BACKGROUND: The study was submitted to evaluate the adsorption/desorption of the active ingredient AC 303268 in sediments. The study was conducted according to the Environmental Protection Agency's Environmental Fate Data Requirements published in Pesticide Assessment

Guidelines, Subdivision N, § 163-1.

CITATION:

Author:	J.A. Mackie
Study Date:	April 7, 1998
Study Title:	"Adsorption/Desorption of [^{14}C]-R107894 in Sediments"
Laboratory Name:	Inveresk Research Tranent EH33 2NE Scotland
Laboratory Report No.:	390723
Sponsor:	Janssen Pharmaceutica N.V. Turnhoutseweg 30 B-2340 Beerse Belgium

OPPTS GUIDELINE NO.: Subdivision N, 163-1

EXECUTIVE SUMMARY:

The adsorption/desorption characteristics of [^{14}C]-R107894 was studied in two freshwater soils, sandy loam and silt loam, and two marine soils, sand and loam, from Scotland in a batch equilibrium experiment. The experiment was conducted in accordance with the EPA Pesticide Assessment Guidelines, Subdivision N, 163-1 and in compliance with the GLP standards as specified under 40 CFR Part 160. The adsorption phase of the study was carried out by equilibrating air-dried/fresh soil with [^{14}C]-R107894 at 0, 54, 109, 268, and 518 ng/g soil for sandy loam and silt loam and at 0, 47, 96, 242, and 484 ng/g soil for sand and loam in the dark at 10 ± 2 °C for 4 hrs for all the soils but sand, which was equilibrated for 8 hrs. The equilibrating solution used was 0.01M $CaCl_2$ or seawater, with a soil/solution ratio of 2g/10g. The desorption phase of the study was carried out by adding a weight of 0.01M calcium chloride or seawater, approximately equal to that removed as supernatant, to each soil type. The tubes were shaken and analyzed as in the adsorption phase.

The supernatant solution after adsorption and desorption was separated by centrifugation. The supernatant was not extracted. [^{14}C]-R107894 residues were analysed by HPLC and TLC. HPLC analysis was carried out using a Hewlett-Packard 1050 series HPLC equipped with an autosampler, u.v. detector and a solvent programmer, connected to an Inertsil Phenyl guard and HPLC column (1 cm and 25 cm x 4.6 mm; 5 μm; Hichrom) and a Packard Flo-One A-100 Series radioactivity monitor. Aliquots of each sample were also submitted to TLC using a silica get 60_{F254} TLC plate and developed in toluene:acetone:methanol:acetic acid. The adsorption parameters were calculated using the Freudlich adsorption isotherm.

The stability of the test material at 10 ± 2°C in 0.01M calcium chloride and seawater was determined by HPLC. Under the test conditions, [^{14}C]-R107894 was found to be unstable. However, the study report stated that these test conditions best reflect those that the test material will enter in the environment and therefore, the Registrant agreed with the Sponsor to proceed with the study. The mass balance at the end of the adsorption phase of the study was 90.99 ± 2.1, 89.45 ± 3.4, 100.5 ± 6.9, and 103.8 ± 2.0% of the applied amount in the sandy loam, silt loam,

sand, and loam soils, respectively. The mass balance at the end of desorption phase was 91.50 ± 1.1, 93.70 ± 4.9, 104.3 ± 7.6, and 99.66 ± 0.9% of the applied amount in sandy loam, silt loam, sand, and loam soils, respectively.

After 4 hr of equilibration for sandy loam, silt loam, loam and 8 hr of equilibration for sand, an average of 98.89, 98.38, 97.48, and 83.18% of the applied amount was adsorbed, respectively. Average adsorption K_d values were 450, 335, 26, and 196 in sandy loam, silt loam, sand, and loam soils, respectively. The average adsorption K_{oc} values were 20440, 16733, 3582, and 5588 in sandy loam, silt loam, sand, and loam soils, respectively. K_f values were 446, 349, 22, and 183 in sandy loam, silt loam, sand, and loam soils, respectively. At the end of the desorption phase, 0.84, 0.88, 9.62, and 1.63% of the adsorbed ^{14}C was desorbed in the sandy loam, silt loam, sand, and loam soils, respectively. Average desorption K_d values were 599, 568, 40, and 299 in sandy loam, silt loam, sand, and loam soils, respectively. The average desorption K_{oc} values were 27229, 28353, 5658, and 8543 for sandy loam, silt loam, sand, and loam soils, respectively. Desorption K_d and K_{oc} values were higher than those obtained for adsorption.

Results Synopsis:

Soil type: Sandy Loam

Amount adsorbed:	98.89%
Adsorption K_d:	450
Adsorption K_{oc}:	20440
Amount desorbed:	0.84%
Desorption K_d:	599
Desorption K_{oc}:	27229

Soil type: Silt Loam

Amount adsorbed:	98.38%
Adsorption K_d:	335
Adsorption K_{oc}:	16733
Amount desorbed:	0.88%
Desorption K_d:	568
Desorption K_{oc}:	28353

Soil type: Sand

Amount adsorbed:	83.18%
Adsorption K_d:	26
Adsorption K_{oc}:	3582
Amount desorbed:	9.62%
Desorption K_d:	40
Desorption K_{oc}:	5658

Soil type: Loam

Amount adsorbed:	97.48%
Adsorption K_d:	196
Adsorption K_{oc}:	5588
Amount desorbed:	1.63%
Desorption K_d:	299
Desorption K_{oc}:	8543

Study Acceptability: This study is classified acceptable and satisfies the guideline requirement for an adsorption/desorption study in soil.

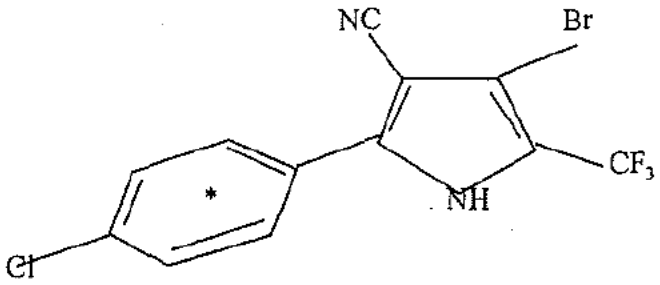
I. MATERIALS AND METHODS

GUIDELINE FOLLOWED:	EPA Pesticide Assessment Guidelines, Subdivision N, 163-1
COMPLIANCE:	Signed and dated statement of GLP compliance as specified in 40 CFR Part 160 included with report. Report also included signed and dated Data

A. MATERIALS:

1. Test Material [Phenyl-^{14}C(U)]-R107894

Chemical Structure:



* Position of Carbon-14 Label

Description: Technical

Purity:

Radiolabelled Lot/Batch No.:	101-077-026.
Analytical purity:	>99% on 6/8/96
Radiochemical purity:	As stated on specification sheet: >99% on 6/8/96 As determined by TLC and HPLC under Iveresk Project Number 390770 (mean radiochemical purity): 98.61%
Specific activity:	26.4 mCi/mmol, 75.4 μCi/mg
Locations of the label:	Radiolabel is located within the phenol ring.

Non-radiolabelled R107894 Lot/Batch No.: AC6943-127

CL 322,250 Lot/Batch No.:	AC9014-97A
CL 325,195 Lot/Batch No.:	AC9014-93B

Storage conditions of test chemieals: The test material was supplied in ethanol. The storage conditions in the laboratory were not provided.

Physico-chemical properties of test material: See Table 1.

Table 1. Physico-chemical properties of R107894

Parameter	Value	Comments
Water solubility	Not provided	--
Vapor pressure/volatility	Not provided	--
UV absorption	Not provided	--
pK_a	Not provided	--
K_{ow}/log K_{ow}	Not provided	--
Stability of Compound at room temperature	Study report states that the exact rate of decomposition is unknown.	--

2. Soil Characteristics: See Tables 2 and 3.

Table 2: Description of soil collection and storage

Description	Soil 1	Soil 2
Freshwater Soils		
Geographic location	Received from Scottish Agricultural College, Auchincruive, Scotland	
Pesticide use history at the collection site	Not provided	
Collection procedures	Not provided	
Sampling depth (cm)	Not provided	
Storage conditions	Not provided	
Storage length	Received on June 26, 1997; Storage length not provided	
Soil preparation (eg: 2 mm sieved; air dried etc.)	Each soil was sieved (2 mm), centrifuged (~1000 rpm, ~15 min) and the moisture content of the soil determined	
Marine Soils		
Geographic location	Received from the Orkney Water Test Centre, Orkney, Scotland	Received from University Marine Biological Station Millport, Isle of Cumbre, Scotland
Pesticide use history at the collection site	Not provided	
Collection procedures	Not provided	
Sampling depth (cm)	Not provided	
Storage conditions	Not provided	
Storage length	Received on June 14, 1997; Storage length not provided	Received on July 4, 1997; Storage length not provided

Description	Soil 1	Soil 2
Soil preparation (eg: 2 mm sieved; air dried etc.)	Each soil was sieved (2 mm), centrifuged (~1000 rpm, ~15 min) and the moisture content of the soil determined	

Table 3: Properties of the soils

Property	Soil 1	Soil 2
Freshwater Soils		
Soil Texture (according to USDA, 1995)	Sandy Loam	Silt Loam
% sand	66.8	20.39
% silt	19.71	59.93
% clay	13.49	19.68
pH	6.5	4.2
Organic carbon (%)	2.2	2
CEC (meq/100 g)	16.9	18.8
Moisture (water content of air dried soil, %)	2.5	1.6
Bulk density (g/cm^3)	Not provided	Not provided
Biomass (mg microbial C/100 g or CFU or other)	Not provided	Not provided
Soil taxonomic classification	Not provided	Not provided
Sol mapping unit (for EPA)	Not provided	Not provided
Marine Soils		
Soil Texture (according to USDA, 1995)	Sand	Silty Clay Loam
% sand	90.04	27.86
% silt	7.55	46.47
% clay	2.41	25.67
pH	7.1	7.7
Organic carbon (%)	0.7	3.5
CEC (meq/100 g)	5.2	15.7
Moisture (water content of air dried soil, %)	0.8	2.1
Bulk density (g/cm^3)	Not provided	Not provided
Biomass (mg microbial C/100 g or CFU or other)	Not provided	Not provided
Soil taxonomic classification	Not provided	Not provided
Sol mapping unit (for EPA)	Not provided	Not provided

C. STUDY DESIGN:

1. Preliminary studies:

Solubility of [^{14}C]-R107894: 100 μL of the test material was diluted in ethanol to a final volume of 5 mL. This solution a (1.17 mL) was transferred to a volumetric flask and the ethanol was removed under a gentle stream of nitrogen. The [^{14}C]-R107894 was then redissolved in 3 mL of acetonitrile. 1 mL of this treatment solution was then added to 100 mL of either 0.01M calcium chloride or seawater to prepare the test solution. The test solution was sonicated for ~15 minutes to aid in dissolution. The final acetonitrile concentration was 1% by volume. Homogeneity of the test solution and the achieved concentration was measured by analysing aliquots of the solution by liquid scintillation counting. The concentration of [^{14}C]-R107894 in 0.01M calcium chloride and seawater was determined to be 0.99 and 0.92 μg/g, respectively. The highest concentration for the main study was to be equivalent to 50% saturation, therefore, the test solutions were diluted to achieve a nominal concentration of 0.5 μg/g. The maximum acetonitrile co-solvent concentration was 0.5%.

Adsorption of [^{14}C]-R107894 to Glass and Filters: 0.5 μg/g solution of [^{14}C]-R107894 in 0.01M calcium chloride were prepared and duplicate aliquots of approximately 10 g were transferred to screw-capped centrifuge tubes and glass vials. The tubes were shaken on an end-over-end shaker (15 inversions per minute) for 16 hours in the dark at 10 ± 2°C. After shaking, duplicate aliquots from each tube were submitted to liquid scintillation counting. The glass vials were incubated at ambient temperature for approximately 16 hours and then duplicate aliquots from each vial were submitted for liquid scintillation counting. No radioactivity was lost from solution from either the centrifuge tubes or the glass vials.

1 μg/g solutions of [^{14}C]-R107894 in 0.01M calcium chloride and seawater were prepared, containing 1% acetonitrile. Each solution was sonicated for approximately 15 minutes and aliquots were submitted for liquid scintillation counting. A sub-sample of each solution was then passed through a 0.45 μm nylon filter and the levels of radioactivity present in the filtrate determined by liquid scintillation counting. The filtrates were re-filtered through new filters and the filtrates re-analyzed. The results indicated that [^{14}C]-R107894 was retained through the initial filtration but successive filtration resulted in a loss of radioactivity. As a result, test solutions were not filtered in the study.

Stability of [^{14}C]-R107894: The stability of the test material at 10 ± 2°C in 0.01M calcium chloride and seawater was determined by HPLC. Under the test conditions, [^{14}C]-R107894 was found to be unstable. However, the study report stated that these test conditions best reflect those that the test material will enter in the environment and therefore, the Registrant agreed with the Sponsor to proceed with the study.

2. Definitive study experimental conditions: See Tables 4 and 5.

Table 4: Study design for the Equilibration and Adsorption phase

[illegible]	soil
Marine and Freshwater Ecosystem	
Condition of soil (air dried/fresh)	air dried
Have these soils been used for other laboratory studies ?	No
Soil (g/replicate)	2 g/replicate
Equilibrium solution used (name and concentration; eg: 0.01N $CaCl_2$)	0.01M calcium chloride or seawater
Control used (with salt solution only) (Yes/No)	Blank tubes prepared with soil and 0.01M calcium chloride or seawater and control tubes prepared with [^{14}C]-R107894 in 0.01M calcium chloride or seawater
Test material concentrations — Analytically measured concentrations (μg a.i./g soil) during equilibration phase	0.01M calcium chloride: 0.458 Seawater: 0.439
Test material concentrations — Analytically measured concentrations (μg a.i./g soil) during analytical phase	0.01M calcium chloride: 0.518, 0.268, 0.109, 0.054 (including 0.5% acetonitrile) Seawater: 0.484, 0.242, 0.096, 0.047 (including 0.5% acetonitrile)
Identity and concentration of co-solvent, if any	0.5% acetonitrile
Soil:solution ratio	2 g soil:10 g solution
Initial pH of the equilibration solution, if provided	Not provided
No. of replications — Controls	Not provided
No. of replications — Treatments	Quadruplicate samples of each soil
Equilibration — Equilibrium Time	Samples taken at 2, 4, 16, 24, and 48 hours
Equilibration — Adsorption Time	4 hrs for sandy loam, silt loam, and loam soil; 8 hrs for sand
Equilibration — Temperature (°C)	10 ± 2°C
Equilibration — Darkness (Yes/No)	Yes
Equilibration — Shaking method	End-over-end shaker (15 inversions per minute)
Equilibration — Shaking time	Samples shaken for a total of 48 hrs; sampled at 2, 4, 16, 24, and 48 hours
Method of separation of supernatant (eg., centrifugation)	Centrifugation
Centrifugation — Speed (rpm or g)	Approximately 1000 rpm

Parameters		Soil
Marine and Fresh Water Systems		
	Duration (min)	Approximately 10 minutes
	Method of separation of soil and solution	Not provided

Table 5: Study design for the desorption phase

Parameters		Soil 1
Were the soil residues from the adsorption phase used? If not, describe the method for adsorption using a separate adsorption Table		Yes
Amount of test material present in the adsorbed state/adsorbed amount (mg a.i./kg soil)	concentration 1	Not provided
	concentration 2	Not provided
	concentration n	Not provided
No. of desorption cycles		1
Equilibration solution and quantity used per treatment for desorption		0.01M calcium chloride or seawater at a weight approximately equal to that removed as supernatant
Soil:solution ratio		Not provided (assumed to be same as adorption)
Replications	Controls	Not provided
	Treatments	Quadruplicate samples of each soil
Desorption equilibration	Time	4 hrs for sandy loam, silt loam, and loam soil; 8 hrs for sand
	Temperature (°C)	10 ± 2°C
	Darkness	Yes
	Shaking method	End-over-end shaker (15 inversions per minute)
	Shaking time	Continuous shaking for 4 hrs or 8 hrs depending on soil
Centrifugation	Speed (rpm or g)	Approximately 1000 rpm
	Duration (min)	Approximately 10 minutes
	Method of separation of soil and solution	Not provided

3. Description of analytical procedures:

Extraction/clean up/concentration methods:
Each soil pellet was extracted three time with 10 mL of acetonitrile for about one hour. The extracts were separated from the residue by centrifugation at 1000 rpm for 10 minutes.

Supernatant samples were not extracted.

Total ^{14}C measurement:
100 μL of Cellulose powder and Combustaid® were added to triplicate portions of each soil pellet prior to combustion in oxygen using a Packard SampleOxidiser, Model 306. The combusted products were adsorbed in Carbo-Sorb®, mixed with Permafluor®E+ and the radioactivity determined by liquid scintillation. Carbon-14 standards, Spec-Chec™, were combusted at the beginning of each day and at regular intervals throughout the day to check combustion and trapping efficiencies. All extracts (100 μL), supernatants (0.5g), and dose solution aliquots (0.5g) were added to scintillant and counted by liquid scintillation counting. Radioactivity was quantified using a liquid scintillation analyzer (Packard 1600TR) with an automatic quench correction by external standard channels ratio.

Identification and quantification of parent compound and transformation products:
HPLC analysis was carried out using a Hewlett-Packard 1050 series HPLC equipped with an autosampler, u.v. detector and a solvent programmer, connected to an Inertsil Phenyl guard and HPLC column (1 cm and 25 cm x 4.6 mm; 5 μm; Hichrom) and a Packard Flo-One A-100 Series radioactivity monitor. Non-radiolabelled reference standards were dissolved in acetonitrile and injected onto the HPLC column individually and as a mixture to determine standard retention times. Quantification of radioactivity was performed by integrating the area under each peak or by submitting fractions to liquid scintillation counting. The recovery of radioactivity injected onto the column for selected samples was measured by collecting the column eluate and submitting aliquots to liquid scintillation counting and comparing the levels recovered with those injected.

Aliquots of each sample were also submitted to TLC using a silica get 60_{F254} TLC plate and developed in toluene:acetone:methanol:acetic acid. The solvent was allowed to develop to a height of 170 mm. Non-radiolabelled R107894, CL 322,250, and CL 325,195 were chromatographed under each sample. Following chromatography, quantification of radioactivity present on TLC plates was performed using a Molecular Dynamics phosphor imager. Standards were visualized by irradiation with u.v. light. Co-chromatography of standard with radioactivity was used for the tentative identification of degradation products.

Detection limits (LOD, LOQ) for the parent compound and transformation products:
The study report stated that a limit of reliable determination, for determination of radioactivity, of 30 d.p.m. above background count rate was instituted in their laboratory. A specific LOD or LOQ was not provided in the study report.

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS:
Three deviations from the test protocol were identified in the study report: (1) the analytical control for 0.01M calcium chloride was analyzed following the addition of an approximately equal volume of acetonitrile, as it was suspected that the test material had precipitated out of solution; (2) tube washes were not conducted as extractions were conducted in the original

centrifuge tubes; and (3) adsorption supernatants samples from sandy loam, silt loam and loam and all desorption supernatants contained insufficient levels of radioactivity to permit chromatographic analysis. The study report stated that these deviations were not considered to have affected the scientific integrity of the study.

B. MASS BALANCE:

The mass balance at the end of adsorption phase of the study was 90.99 ± 2.1, 89.45 ± 3.4, 100.5 ± 6.8, and 103.8 ± 2.0% of the applied amount in the sandy loam, silt loam, sand, and loam, respectively. The mass balance at the end of desorption phase was 91.50 ± 1.1, 93.70 ± 4.9, 104.3 ± 7.6, and 99.66 ± 0.9% of the applied amount in sandy loam, silt loam, sand, and loam, respectively.

Table 6: Recovery of [^{14}C]-R107894, expressed as percentage of applied radioactivity, in soil after adsorption/desorption (mean ± s.d.)

Matrices	Sandy Loam	Silt Loam	Sand	Loam
At the end of the adsorption phase				
Adsorption supernatant	1.02 ± 0.13	1.26 ± 0.04	16.02 ± 0.29	2.34 ± 0.13
Extractable Radioactivity	85.76 ± 1.80	83.68 ± 3.49	75.27 ± 5.98	88.84 ± 1.70
Non-extractable residues	4.21 ± 0.13	4.51 ± 0.02	9.22 ± 1.14	12.65 ± 0.38
Total recovery	90.99 ± 2.05	89.45 ± 3.43	100.50 ± 6.82	103.83 ± 1.95
At the end of the desorption phase				
Adsorption supernatant	1.01 ± 0.01	1.97 ± 0.86	15.79 ± 0.04	2.18 ± 0.06
Desorption Supernatant	0.75	0.82 ± 0.03	9.13 ± 0.08	1.36 ± 0.04
Extractable Radioactivity	84.73 ± 1.12	86.68 ± 5.42	70.70 ± 6.94	84.19 ± 0.26
Non-extractable residues	5.02 ± 0.01	4.23 ± 0.33	8.64 ± 0.66	11.94 ± 1.21
Total recovery	91.50 ± 1.14	93.70 ± 4.86	104.25 ± 7.55	99.66 ± 0.85

Table 7: Concentration of [^{14}C]-R107894 in the solid and liquid phases at the end of adsorption equilibration period (mean ± s.d.)

Concentration (ng/g)	Sandy Loam			Silt Loam			Sand			Loam		
	Soil Conc.[a] (ng/g)	Solution Conc. (ng/g)	% adsorbed[b]	Soil Conc.[a] (ng/g)	Solution Conc. (ng/g)	% adsorbed[b]	Soil Conc.[a] (ng/g)	Solution Conc. (ng/g)	% adsorbed[b]	Soil Conc.[a] (ng/g)	Solution Conc. (ng/g)	% adsorbed[b]
Concentration 1	2603 ± 19.1	5.67 ± 0.06	98.91 ± 0.01	2533 ± 21.9	10.88 ± 4.50	97.90 ± 0.86	2043 ± 19.8	80.35 ± 0.06	83.40 ± 0.01	2355 ± 2.8	12.0 ± 0.32	97.53 ± 0.06
Concentration 2	1336 ± 6.36	2.98 ± 0.17	98.89 ± 0.06	1333 ± 1.41	3.47 ± 0.22	98.71 ± 0.08	1031 ± 2.12	38.92 ± 0.21	83.92 ± 0.08	1195 ± 17.7	5.46 ± 0.08	97.75 ± 0.04
Concentration 3	538 ± 2.83	1.16 ± 0.03	98.94 ± 0.02	536 ± 0.71	1.32 ± 0.01	98.79 ± 0.01	402 ± 1.41	16.34 ± 0.40	82.98 ± 0.40	470 ± 11.3	2.52 ± 0.06	97.38 ± 0.07
Concentration 4	273 ± 3.54	0.64 ± 0.04	98.82 ± 0.08	268 ± 6.36	1.02 ± 0.45	98.11 ± 0.83	197 ± 0.71	8.27 ± 0.03	82.41 ± 0.04	232 ± 2.83	1.29 ± 0.06	97.26 ± 0.12

[a] amount on soil residue is measured by soil residue analysis
[b] % of applied radioactivity which is adsorbed

Table 8: Concentration of [^{14}C]-R107894 in the solid and liquid phases at the end of desorption equilibration period (mean ± s.d.)

Concentration (ng/g)	Sandy Loam			Silt Loam			Sand			Loam		
	Soil Conc.[a] (ng/g)	Solution Conc. (ng/g)	% desorbed[b]	Snil Conc.[a] (ng/g)	Solution Conc. (ng/g)	% desorbed[b]	Soil Conc.[a] (ng/g)	Snlution Conc. (ng/g)	% desorbed[b]	Soil Conc.[a] (ng/g)	Solution Conc. (ng/g)	% desorbed[b]
Concentration 1	2584 ± 19.1	4.27 ± 0.01	0.83 ± 0.01	2512 ± 22.6	4.58 ± 0.06	0.90 ± 0.02	1825 ± 19.1	46.88 ± 0.39	9.72 ± 0.08	2323 ± 4.2	7.84 ± 0.30	1.62 ± 0.06
Concentration 2	1326 ± 8.49	2.22 ± 0.29	0.83 ± 0.11	1323 ± 2.83	2.24 ± 0.22	0.84 ± 0.08	929 ± 4.95	22.12 ± 0.54	9.10 ± 0.23	1179 ± 18.4	3.72 ±0.16	1.54 ± 0.05
Concentration 3	534 ± 2.83	0.83 ± 0.07	0.76 ± 0.06	532 ± 1.41	0.89 ± 0.09	0.82 ± 0.09	364 ± 3.54	8.67 ± 0.25	9.12 ± 0.35	464 ± 10.6	1.51 ± 0.01	1.57 ± 0.01
Concentration 4	271 ± 3.54	0.50 ± 0.01	0.93 ± 0.02	265 ± 7.07	0.53 ± 0.14	0.99 ± 0.28	174 ± 2.12	4.89 ± 0.18	10.52 ± 0.47	228 ± 2.83	0.84 ± 0.09	1.80 ± 0.16

a Each value in the solid phase is the amount present after 1 desorption and each value in the solution phase is the total amount desorbed.
b % of applied radioactivity which is desorbed

Table 9: Adsorption and desorption constants of [^{14}C]-R107894 in the soils

Soil	Adsorption					Desorption	
	K_d	K_{oc}	K_f	R^2	1/N	K_d	K_{oc}
Sandy loam--							
Concentration 1	460	20883				605	27502
Concentration 2	449	20401	446	1	1.031	604	27458
Concentration 3	464	21089				646	29358
Concentration 4	427	19388				541	24596
Silt loam--							
Concentration 1	255	12749				549	27428
Concentration 2	386	19274	349	0.967	0.882	595	29744
Concentration 3	406	20286				605	30224
Concentration 4	293	14622				521	26016
Sand--							
Concentration 1	26	3633				39	5562
Concentration 2	27	3783	22	1	1.046	42	5999
Concentration 3	25	3516				42	5997
Concentration 4	24	3394				36	5073
Loam--							
Concentration 1	197	5611				297	8478
Concentration 2	219	6257	183	0.998	1.049	318	9079
Concentration 3	187	5340				307	8771
Concentration 4	180	5142				275	7844

K_d -Adsorption and desorption coefficients
K_{oc} - Coefficient adsorption per organic carbon (K_d x 100/% organic carbon)
K - Freundlich adsorption coefficients
R^2 - Regression coefficient of Freundlich equation
1/N -Slope of Freundlich adsorption isotherms

C. ADSORPTION:

Adsorption remained the same with increasing concentration. After 4 hr of equilibration for sandy loam, silt loam, loam and 8 hr of equilibration for sand, an average of 98.89, 98.38, 97.48, and 83.18% of the applied amount was adsorbed, respectively. Average adsorption K_d values were 450, 335, 26, and 196 in sandy loam, silt loam, sand, and loam soils, respectively. The average adsorption K_{oc} values were 20440, 16733, 3582, and 5588 in sandy loam, silt loam, sand, and loam soils, respectively. K_f values were 446, 349, 22, and 183 in sandy loam, silt loam, sand, and loam soils, respectively.

D. DESORPTION:

At the end of the desorption phase, 0.84, 0.88, 9.62, and 1.63% of the adsorbed ^{14}C was desorbed in the sandy loam, silt loam, sand, and loam soils, respectively. Average desorption K_d values were 599, 568, 40, and 299 in sandy loam, silt loam, sand, and loam, respectively. The average desorption K_{oc} values were 27229, 28353, 5658, and 8543 for sandy loam, silt loam, sand, and loam, respectively. Desorption K_d and K_{oc} values were higher than those obtained for adsorption.

III. STUDY DEFICIENCIES:

The following study deficiencies were noted:

- The study report stated that controls were included in the study but their values were not

provided. Only qualitative statements concerning the controls were included in the report.

- Storage conditions in the laboratory were not provided.
- A detection limit was not provided in the study report.
- In the desorption phase study design, the amount of test material present in the adsorbed state/adsorbed amount (mg ai/kg soil) was not provided.
- Physico-chemical properties of the test material were not provided.

IV. REVIEWER'S COMMENTS:
The following issues of concern were noted:

- The raw data were not provided and therefore, the results presented could not be verified.

V. REFERENCES:
No reference were used in either the study or the evaluation.

Conclusion: RASSB concludes that this missing information does not alter the acceptability of the study. The study is acceptable.

DECISION PKG. NO. 22066 SUBM. DUE DATE _____

SUBMISSION BAR CODE # 634182 REVIEWER KV

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 43813-ET PM 33 ACTION CODE 115

DESCRIPTOR _____ **FQPA**___ **NFQPA**___

[ ] CHILD RESISTANT PACKAGING: [ ] REQUIRED [ ] NOT REQUIRED

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
03/27/03	03/28/03	03/28/03

METHOD OF SUPPORT

[ ] CITE-ALL [ ] SELECTIVE
[ ] NOT SUBMITTED [ ] N/A

FORMULATORS EXEMPTION

[ ] SUBMITTED [ ] NOT SUBMITTED
[ ] N/A

REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
EFFICACY				
ACUTE TOX.				
RASSB TOX.				
ENVIRON. FATE				
FISH/WILDLIFE				
OTHER: _____ :				

STATUS _____

RESPONSE CODE 38 RESPONSE DATE 10-03-03

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OCT 03 2003

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. Bill Goodwine
Janssen Pharmaceutica, Inc.
11215 Trenton-Harbourton Road
Titusville, NJ 08560

Subject: ECONEA Technical
EPA File Number 43813-ET
Your Submission Dated September 30th, 2003
EPA Received Date October 3rd ,2003

The submission referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, to obtain approval for the leaching rate study for the active ingredients RH-287 and AC 303268 in Sigma Nexxium 20 paint, is acceptable.

This study is acceptable and reflects the guidelines specified for the ASTM Method D5108-90 for aqueous availability. The Agency recommends that the special leaching study for AC 303268 and RH-287 antifoulant agents be accepted in support of registration of the product, Sigma Nexxium 20 paint. The study was conducted according to the ASTM D5108-90 Method modified for RH-287 and AC 303268-based paints.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,

Marshall Swindell
Product Manager 33
Regulatory Management Branch 1
Antimicrobial Division(7510C)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 17 2003

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Review of Leaching Study for Sigma Nexxium 20 Paint Containing AC 303268 and RH-287 Antifoulants

TO: Marshall Swindell, Product Manager Team 33
Regulatory Management Branch I
Antimicrobials Division(7510C)

FROM: Robert Quick, Chemist Robert Quick
Risk Assessment and Science Support Branch
Antimicrobials Division(7510C)

THRU: Norm Cook, Chief 9.17.03
Risk Assessment and Science Support Branch
Antimicrobials Division(7510C)

ID#: 043813-ET

DP BARCODE: 456732-01

SUBMISSION: S631626

CASE NO.: 072289

PC CODE: 119093

CAS#: 122454-29-9

CHEMICAL NAME: 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-trifluoromethyl)

Introduction:

Janssen Pharmaceuticaa has submitted a release rate study for the active ingredients in a marine antifoulant paint. The name of the paint is Sigma Nexxium 20 Paint. The paint contains Sea Nine™ 211 and AFO28 antifoulant chemicals. Sea Nine 211 is also known as RH-287 or 4,5-dichloro-2-n-octyl-3(2H)-isothiazolone. AFO28 is AC 303268 or 1H-Pyrrole-3-caronitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl). The "bean sheet" is for the chemical, 1H-Prrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoro), and the instructions are, "Please review new chemical ecotox. data for acceptability". The release rate(leaching) data are for both chemicals. The data were submitted as a part of the data packages for the new chemical AC 303268. A number of data packages for AC 303268 are being reviewed under different "bean sheets" for the various scientific disciplines.

Background:

AC 303268 is a new chemical. No label is submitted with this data package containing this leaching study. The co-active ingredient in the formulation is also known as Sea Nine-211. That chemical is already registered as an antifoulant.

Conclusions:

1a. The average leach rate for AC 303268 between day 21 and day 45 was 8.56 $\mu g/cm^2$ /day.
b. The cumulative leach rate for AC 303268 through day 1 was 12.9 $\mu g/cm^2$ and through day 45 was 454 $\mu g/cm^2$.

2a. The average leach rate for RH-287 between day 21 and day 45 was 35.7 $\mu g/cm^2$ /day.
b. The cumulative leach rate for RH-287 through day 1 was 57.5 $\mu g/cm^2$ and through day 45 was 1813 $\mu g/cm^2$.

Recommendations:

This study is acceptable and reflects the guidelines specified for the ASTM Method D5108-90 for aqueous availability. RASSB recommends that the special leaching study for AC 303268 and RH-287 antifouling agents be accepted in support of registration of the product, Sigma Nexxium 20 Paint.

SPECIAL LEACHING STUDY
DATA EVALUATION REPORT

PRODUCT FORMULATION: Sigma Nexxium 20 Paint
ACTIVE INGREDIENT: 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chloropropyl)-5-(trifluoromethyl), also known as AC 303268

BACKGROUND: The study was submitted to determine the leach rates of the active ingredients

RH-287 and AC 303268 in Sigma Nexxium 20 paint. The study was conducted according to the ASTM D5108-90 Method modified for RH-287 and AC 303268-based paints..

CITATION:

Author: David J. Sinning
Date: February 21, 2002

Title: *Leach Rate Determination of Sigma Nexxium 20 Paint Containing Sea Nine™ 211 and AFO28 Antifoulings*
Laboratory: Case Consulting Laboratories, Inc., 622, Route Ten, Whippany, New Jersey 07981
Sponsor: Sigma Coatings USA B.V., P.O. Box 816, 1401 Destrehan Avenue, Harvey Louisiana 70059
Study Date: October 15, 2001 to February 21, 2002

OPPTS GUIDELINE NO: None

EXECUTIVE SUMMARY:

The leach rate determination of Sigma Nexxium 20 Paint was studied using the ASTM D5108-90 Method: *Standard Test Method for Organotin Release Rates of Antifouling Coating Systems in Sea Water*, specifically designed for antifoulants. This test method was modified for Sea Nine™ 211 (RH-287) and AC 303268 based paints. The study was conducted to determine the rate at which Sea Nine™ 211 (RH-287) and AC 303268 are released from Sigma Nexxium 20 Paint. The study was conducted in synthetic sea water, which was prepared according to ASTM D 114, Section 6 Standard Method, at 25 ± 2°C. Salinity of the synthetic sea water was maintained at 30 to 35 ppt and a pH of 7.8 to 8.2. The study of leach rate measurement was conducted for 45 days. The experiments were carried out in compliance with the EPA GLP standard, 40 CFR Part 160. A pseudo steady-state leach rate was attained after 21 days and 38 days for the AC 303268 and RH-287 samples, respectively. The average leach rate of AC 303268 from the paint between day 21 and day 45 was 8.56 $\mu g/cm^2$/day with a standard deviation of 1.2 $\mu g/cm^2$/day. The cumulative release of AC 303268 from the paint was 12.9 $\mu g/cm^2$ through day 1 and 454 $\mu g/cm^2$ through day 45. For RH-287, the average leach rate between day 21 and day 45 was 35.7 $\mu g/cm^2$/day with a standard deviation of 8.4 $\mu g/cm^2$/day. The cumulative release of RH-287 from the paint was 57.5 $\mu g/cm^2$ through day 1 and 1813 through day 45.

Sigma Nexxium 20 Paint was applied to polycarbonate cylinders measuring 2.5 inches (6.4 cm) in diameter (cylinder length not reported). The area that the Sigma Nexxium 20 paint was applied to on the cylinder was 200 cm^2 with a film thickness of at least 0.004 inches (100 μm).

Cylinders were put in the holding tank (food-grade polyolefin) of 100 liter capacity. Synthetic sea water was continuously circulated through the tank, an activated carbon filter and a chelating resin filter at a rate of 5 L/min. Leach rates were measured by exposing the cylinders to 1500 mL

of synthetic sea water and rotating the cylinders for 60 minutes at 60 ± 5 rpm. The leach rates were measured on days 1, 3, 7, 10, 14, 21, 24, 28, 31, 35, 38, 42, and 45.

Samples of the leached Sigma Nexxium 20 Paint were collected and analyzed for Sea Nine™ 211 (RH-287) and AC 303268 by HPLC. The study did not report the identification of any transformation products.

The study is acceptable and reflects the guidelines specified by the ASTM Method D5108-90 for aqueous availability.

RESULTS SYNOPSIS:

Average Leach Rate (AC 303268) between day 21 and day 45:	8.56 μg/cm^2 /day
Cumulative Leach Rate (AC 303268) between day 1 and day 45:	12.9 to 454 μg/cm^2
Average Leach Rate (RH-287) between day 21 and day 45:	35.7 μg/cm^2 /day
Cumulative Leach Rate (RH-287) between day 1 and day 45:	57.5 to 1813 μg/cm^2

I. MATERIALS AND METHODS

Guideline followed: The study followed ASTM Standard Method D5108-90: *Standard Test Method for Organotin Release Rates of Antifouling Coating Systems in Sea Water*.

Compliance: The study was performed in compliance with GLP standards as specified in 40 CFR Part 160. Signed and dated GLP, Quality Assurance, and Data Confidentiality Statements were provided.

A. Materials:

1) Test Material: Sigma Nexxium 20 Paint

Description: The test substance is a antifouling paint, redbrown in color containing the active ingredients Sea Nine™ 211 (3.43%) and AC 303268 (3.68%). The material was supplied by Sigma Coatings USA Paints B.V. (Batch No. 1020573506).

Purity: Analytical purity:
Sea Nine™ 211 (RH-287) - 99.86%
AC303268 - 94.6%

The physical-chemical properties of Sigma Nexxium 20 Paint were not reported.

2) Synthetic Sea Water Solution:

The synthetic sea water was prepared according to ASTM Method D 1141, Section 6, and stored in a 100-L tank (food-grade polyolefin) at 25 ± 2°C. The water was continually pumped through the tank, an activated carbon filter, and a chelating resin filter at a rate of 5 L/min.

B. Experimental Conditions:

1) Experimental Conditions:

Duration of study:	October 15, 2001 to February 21, 2002
No. of replications:	3 replicates
pH of the synthetic sea water:	7.8 to 8.2
Temperature of the sea water:	25 ± 2°C
Salinity of sea water:	30 to 35 ppt
Type of cylinders used:	Polycarbonate cylinders (2.5 inch diameter)
Area of cylinders painted:	200 cm^2
Rate (rpm)of cylinder rotations:	60 ± 5 rpm
Duration of cylinder rotation:	60 minutes
Paint thickness:	At least 0.004 inches (100 μm)

2) Sampling:

The cylinders were removed from the holding tanks on days 1, 3, 7, 10, 14, 21, 24, 28, 31, 35, 38, 42 and 45. The cylinders were placed in a measuring container holding 1,500 mL of synthetic sea water at 25 ± 2°C and were rotated in the container at 60 ± 5 rpm for 60 minutes. After one hour, 45 mL of the exposed sea water sample was measured into 2-oz. glass bottles and 5 mL of methanol was added to each bottle. The bottles were then sealed with polyseal caps and refrigerated until analysis. The cylinders were placed back into the holding tanks until the next leaching interval.

C. Analytical Methods:

The samples were analyzed by HPLC with detection limits of 22.7 ppb and 15.6 ppb for AC 303268 and RH-287, respectively. A reference standard and spike sample were injected with each sample run. The HPLC analysis was conducted under the following operating conditions:

Pump:	Knauer Model 364.00
Detector:	Knauer Variable Wavelength Detector Model 731.87
Autosampler:	Shimadzu Model SIL-10A
Column:	Phenomenex Luna, C-18(2), 5 μm, 250 x 4.6 mm
Flow Rate:	1.0 mL/min.

Injection Volume: 400 µL
Detection: UV 275 nm
Gradient:

Time	% Solution A (0.01 M Acetate)	% Solution B (80:20, Acetonitrile:0.05 M Acetate)
0.0	100	0
0.1	0	100
20.0	0	100
20.1	100	0
30	100	0

Calculations and Results -

The release rates of AC 303268 and RH-287 for each sample were calculated by using the following equation:

$$R = (C \times V \times D) \div (T \times A) = C \times 0.18$$

where: R = Release rate, µg/cm²/day
C = Concentration of AC 303268 or RH-287 in the release rate sample, µg/L
V = Volume of synthetic sea water in measuring container, 1.5 L
D = 24 hours/day
T = Rotation time of painted cylinder, 1 hour
A = Area of painted surface on the cylinder, cm² (diameter of cylinder (cm) x length of painted band on cylinder (cm) x π), 200 cm²

Cumulative release rates of AC 303268 and RH-287 were calculated for each sampling day by multiplying the average release rate at each sampling day by the number of days in the interval and then summing the values. The equation used as shown in ASTM Standard Test Method D 5018-90, is as follows:

$$CR = R_1 + (2 \times R_3) + (4 \times R_7) + (3 \times R_{10}) + (4 \times R_{14}) + (7 \times R_{21}) + (3 \times R_{24}) + (4 \times R_{28}) + (3 \times R_{31}) + (7 \times R_{38}) + (4 \times R_{42}) + (3 \times R_{45})$$

where: CR = Cumulative release rate, µg/cm²
R_1, R_3, R_7, etc. = Day 1 Release Rate, Day 3 Release Rate, Day 7 Release Rate, etc.

II. RESULTS AND DISCUSSION

A. Test Conditions:

The study author reported that the temperature was maintained at 25 ± 2°C, the pH ranged from 7.8 to 8.2 and the salinity was maintained between 30 to 35 ppt; however, no raw data were reported to support this information.

B. Anomalies:

The study author reported that the samples collected from day 35 were not analyzed due to technical problems with the HPLC system. Therefore, the cumulative release rate calculations were corrected to account for this. The study author stated this had no effect on the leach rate determination.

III. COMMENTS

1. Raw data for the temperature, pH and salinity of the test system were not provided.

2. The painted test cylinders were allowed to dry for 7 days prior to the test initiation; however, the drying temperature was not reported. The ASTM Method specifies a drying temperature of 23-27°C.

3. The manufacturing date and storage information of the paint was not provided. The ASTM Method specifies that the paint be manufactured a minimum of 7 days prior to testing and test paints should not be allowed to age beyond the manufacturer's recommended shelf-life.

RASSB concludes that this missing information does not alter the acceptability of the study. The study is acceptable.

DP #: (289031) Decision #: 220066

DATA PACKAGE BEAN SHEET

Date: 22-Sep-2003

* * * Registration Information * * *

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA

Risk Manager: RM 33 - Dennis - Edwards Jr - (703) 308-8087 Room# CM-2 308S

Risk Manager Reviewer: Karen Leavy - KLEAVY

Sent Date: 19-Mar-2003 Calculated Due Date: 18-Sep-2003 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: NEW INGREDIENT;NEW REGISTRATION;NON-FOOD/FEED USE;

Ingredients: 119093

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 20-Mar-2003 Due Back:

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title:

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

Assigned To		Date In	Date Out	
Organization:	AD / RASSB	20-Mar-2003	17-Sep-2003	Administrative Due Date: 18-Jul-2003
Team Name:				Negotiated Due Date:
Reviewer Name:	Quick, Bob	15-Apr-2003	15-Sep-2003	Projected Completion Date:
Contractor Name:				

* * * Studies Sent for Review * * *

Printed on Page 2

* * * Additional Data Package for this Decision * * *

Printed on Page 3

* * * Data Package Instructions * * *

Please review new chemical ecotox. data for acceptability.
(WJAKOB)

DP#: (289031) *** Additional Data Package for this Decision *** Decision#: (220066)

DP #	Division/Branch	Date Sent	Date Due	Instructions?	CSF	label
289021	AD / RASSB	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289021	AD / RMB1	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289026	AD / RASSB	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289026	AD / RMB1	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289027	AD / RASSB	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289027	AD / RMB1	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289029	AD / RMB1	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289029	AD / RASSB	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289033	AD / RMB1	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289033	AD / RASSB	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
290345	AD / RASSB	22-Sep-2003	22-Sep-2003	○ Yes ○ No	○ Yes ● No	○ Yes ● No
290345	AD / RMB1	22-Sep-2003	22-Sep-2003	○ Yes ○ No	○ Yes ● No	○ Yes ● No
292015	AD / RASSB	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
292015	AD / RASSB	22-Sep-2003	22-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No

DP #: (289033) Decision #: 220066

DATA PACKAGE BEAN SHEET

Date: 03-Sep-2003

* * * Registration Information * * *

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA

Risk Manager: RM 33 - Marshall - Swindell - (703) 308-6341 Room# CM-2 308H

Risk Manager Reviewer: Karen Leavy - KLEAVY

Sent Date: 19-Mar-2003 Calculated Due Date: 18-Sep-2003 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: NEW INGREDIENT;NEW REGISTRATION;NON-FOOD/FEED USE;

Ingredients: t19093

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 20-Mar-2003 Due Back:

DP Ingredient: t19093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title:

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

	Assigned To	Date In	Date Out	
Organization:	AD / RASSB	20-Mar-2003	27-Aug-2003	Administrative Due Date: 18-Jul-2003
Team Name:				Negotiated Due Date:
Reviewer Name:	Quick, Bob	15-Apr-2003	25-Aug-2003	Projected Completion Date:
Contractor Name:				

* * * Studies Sent for Review * * *

Printed on Page 2

* * * Additional Data Package for this Decision * * *

Printed on Page 3

* * * Data Package Instructions * * *

Please review new chemical product chemistry data foracceptability.(BQUICK)

DP#: (289033) *** Additional Data Package for this Decision *** Decision#: (220066)

DP #	Division/Branch	Date Sent	Date Due	Instructions?	CSF	label
289021	AD / RASSB	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289021	AD / RMB1	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289026	AD / RASSB	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289026	AD / RMB1	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289027	AD / RASSB	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289027	AD / RMB1	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289029	AD / RMB1	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289029	AD / RASSB	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289031	AD / RASSB	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
289031	AD / RMB1	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
290345	AD / RASSB	03-Sep-2003	03-Sep-2003	○ Yes ○ No	○ Yes ● No	○ Yes ● No
290345	AD / RMB1	03-Sep-2003	03-Sep-2003	○ Yes ○ No	○ Yes ● No	○ Yes ● No
292015	AD / RASSB	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No
292015	AD / RASSB	03-Sep-2003	03-Sep-2003	○ Yes ○ No	● Yes ○ No	● Yes ○ No

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. Bill Goodwine
Janssen Pharmaceutica, Inc.
11215 Trenton-Harbourton Road
Titusville, NJ 08560

Subject: ECONEA Technical
EPA File Number 43813-ET
Your Application Dated March 27th, 2003
EPA Received Date March 28th ,2003

The application referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, is incomplete.

Upon conducting a new chemical screen on the submitted materials for the intended use pattern and the following comments apply:

The nine studies provided for the product chemistry DER included most of the information required by the Group A and B, Series 830 Guidelines. Ten characteristics of the test substance, required by the guidelines, were not provided in the study Reports, including: (1) Description of Formulation Process, (2) Oxidation /Reduction: Chemical Incompatability, (3) Flammability/ Flame Extension, (4) Explodibility, (5) Miscibility, (6) Corrosion Characteristics, (7) Dielectric Breakdown Voltage, (8) Viscosity, (9) Boiling Point/Boiling Range, (10) Particle Size, Fiber Length and Dimeter Distribution and are not required for this TGAI powder.

The data are adequate to support registration of the TGAI.

A complete copy of the science memo is enclosed for your records.

The product mentioned above has not passed the chemical screen; however, based upon our agreement to initiate a review of all submitted data, except toxicity data due to missing studies, data reviews are still being processed.

As per our letter of March 18th, 2003, due to the unusual circumstances associated with this new active ingredient, the Agency will place the environmental and ecological effects data as well as the chemistry and end-use application into review in the absence of a complete data package. Normally, a new active ingredient submission must be a complete package before the Agency will start its review process.

Please note that when toxicology data are submitted they will be placed into review on a track independent of the environmental and other reviews.

The product may not be lawfully distributed in interstate commerce until the above discrepancies have been fulfilled.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,

Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 27 2003

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Product Chemistry Review for AC 303268 TGAI

TO: Marshall Swindell Product Manager Team 33
Regulatory Management Branch I
Antimicrobials Division(7510C)

FROM: Robert Quick, Chemist
Risk Assessment and Science Support Branch
Antimicrobials Division(7510C)

THRU: Norm Cook, Chief 08.27.03
Risk Assessment and Science Support Branch
Antimicrobials Division(7510C)

ID#: 043813-ET

DP BARCODE: D289033

SUBMISSION: S631626

CASE NO.: 072289

PC CODE: 119093

CAS#: 122454-29-9

MRID#S: 456958-01C, 456958-02C, 456739-01C, 456739-02C, 456739-03C, 456739-04C, 456739-06, 456739-07, 456739-05C

Introduction:

Janssen Pharmaceutica has submitted a data package for registration of the Technical Grade Active Ingredient(TGAI), of AC303268(EPA Registration No. 043813-ET. The data package contains product chemistry data to fulfil the data requirements for the following OPPTS product chemistry guidelines: 830.1550; 830.1600; 830.1620; 830.1670; 830.1700; 830.1750; 830.1800; 830.7370, 830.6313, 830.7950; 830.6302; 830.6303; 830.6304; 830.7000; 830.7050; 830.830.7100; 830.7200; 830.7300; 830.7370; 830.7550; 830.7560; 830.7570; 830.7840; 830.7860 and 830.7860.

The submission for this "bean" contains only the above cited product chemistry studies.

Background: This is the first registration for the new chemical, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl). This memorandum addresses the product chemistry data for the technical grade active ingredient. Other memoranda will review data for other scientific disciplines.

This chemical is intended for use in antifoulant products.

Conclusions:

1. The product chemistry data requirements are fulfilled with the following exception:

a. The registrant has declared the enforcement analytical method to be confidential. Analytical methods submitted to the Agency for enforcement purposes cannot be claimed as confidential. If the MRID# containing the analytical method contains confidential information, then the analytical method should be removed from that MRID#.

PRODUCT CHEMISTRY
DATA EVALUATION RECORD

Product Formulation: Technical AC 303268
Active Ingredients: 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl), also known as CL 303268 and R107894

BACKGROUND

Nine studies were submitted on the product chemistry of the technical grade active ingredient, CL 303,268 or 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl), in support of registration. These studies were reviewed following the Group A: Series 830-Product Identity, Composition and Analysis Test Guidelines and the Group B:

Series 830-Physical and Chemical Properties. The seven studies include: (1) *Preliminary Analysis and Certification of Ingredient Limits for the Technical Grade of AC 303268* (MRID 456958-01C), (2) *Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303268, Description of Materials Used to Produce Product, Description of Production Process* (MRID 456958-02C), (3) *Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303268, Description of the Formation of Impurities* (MRID 456739-01C), (4) *Validation of the Ion Chromatographic Method M-3417.01 to Assay for Triethylamine (TEA) in the CL 303268 Technical Grade Active Ingredient (TGAI)* (MRID 456739-02C), (5) *Validation of HRGC Method M-3467.01 to Assay for CL 312264 and CL 322697 in the Technical Grade of AC 303268* (MRID 456739-03C), (6) *Validation of High Performance Liquid Chromatographic Method M-3397.03 to Assay for the Minor Components in CL 303268 Technical Grade Active Ingredient* (MRID 456739-04C);(7) *Validation of the High Performance Liquid Chromatographic Method M-3408 to Assay for CL 303268 in the Technical Grade Active Ingredient (TGAI)* (MRID 456739-05C), (8) *R107894: Determination of the Physico-Chemical Properties (pH, pKa and EC Tests A4, A6 and A8* (MRID 456739-06), and (9) *R107894: Determination of Physico-Chemical Properties* (MRID 456739-07).

FINDINGS

A. Product Identity, Composition and Analysis

1. Product Identity and Composition (Guideline #830.1550; Required)

1.	Name:	Technical AC 303268
2.	IUPAC Name:	1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)
3.	Other Names:	CL 303268, R107894
4.	CAS Number:	122454-29-9
5.	Empirical Formula:	$C_{12}H_5F_3N_2BrClN$

2. Description of Material Used to Produce the Product (Guideline #830.1600; Required)

See Confidential Appendix.

3. Description of Production Process (Guideline #830.1620; Required - TGAI only)

See Confidential Appendix.

4. Description of Formulation Process (Guideline #830.1650; Required for an end product.)

This memo addresses the product chemistry for the TGAI. The production process for the TGAI is discussed above. There is no formulation process for the TGAI.

5. Discussion of Formation of Impurities (Guideline #830.1670, Required - TGAI only)

The preparation of each of the intermediates and final product are discussed separately. For each, the intended reaction and manufacturing procedure are given, as well as a discussion of known and potential impurities from starting materials, side reactions, reactions of side products of the previous step, and further reactions of impurities in the starting materials (MRID 456739-01C).

The data are adequate to support registration of the TGAI.

See Confidential Appendix.

6. Preliminary Analysis (Guideline #830.1700; Required TGAI only)

The data are adequate to support registration of the TGAI.

See Confidential Appendix.

7. Certified Limits (Guideline #830.1750; Required)

The certified limits for CL 303268 TGAI and the minor components were provided in MRID 456958-01C. However, these results were deemed confidential by the registrants.

The analytical method used in the analyses to determine the certified limits is described below under "Enforcement Analytical Method".

The data are adequate to support registration.

8. Enforcement Analytical Method (Guideline #830.1800; Required)

The active ingredient is determined using HPLC method M-3408.01. The CL 303268 minor components in the CL 303268 TGAI are determined using HPLC method M-3397.04 and HRGC method M-3467.02. Residual solvents, acetonitrile and N,N-dimethylformamide, are assayed using HRGC method M-3421 and no residual solvents were detected. The level of triethylamine is determined using ion chromatography method M-3417.01. The water content is determined using coulometric Karl Fischer method M-2372.02. The ash level is determined using method M-2215.01. The quantification of a phosphorous compound proposed to be CL 999425 is achieved using NMR method M-2103.01.

This validation study demonstrated that HPLC method M-3408 for the analysis of CL 303268 in AC 303268 TGAI is a valid method with regard to specificity, accuracy, precision and ruggedness. The analytical standard and test substance were tested and CL 303268 was found to be stable in both solutions for at least 14 days. The system suitability parameters described in the method were also confirmed. The specificity of the method was validated by the sufficient

resolution of CL 303268 from potential minor component CL 303267 and by the good homogeneity of the CL 303268 peak. The accuracy of the method was verified by performing a linearity test for CL 303268 using least squares analysis. The precision of the method was demonstrated by the repeatability and reproducibility of the assay results for CL 303268. The ruggedness of the method was demonstrated by the reproducibility of the assay results obtained while varying the mobile phase, pH, column temperature and the mobile phase composition. The solution stability was determined by analyzing the analytical standard and test substance solutions on the day of preparation and then reanalyzing the solutions two weeks after preparation.

The identity of the CL-designated chemicals can be found in MRID# 456739-01C.

The method appears to be adequate to support the registration of the TGAI for this chemical.

B. Physical and Chemical Properties

1. Color (Guideline #830.6302; Required)

The color was determined as pale yellow-brown (Munsell reference 5Y8.5/4).

2. Physical State (Guideline #830.6303; Required)

The test substance was identified as a powder.

3. Odor (Guideline #830.6304; Required)

The test substance has a slightly sweet, marzipan-like odor.

4. Stability to Sunlight, Normal and Elevated Temperatures, Metals/Metal Ions (Guideline #830.6313; Required)

The test substance was stable after incubation for 14 days at 54°C and is stable in the presence of copper and iron. the data are adequate to support registration of the TGAI.

5. Oxidation/Reduction: Chemical Incompatibility (Guideline #830.6314; Required)

The registrant did not provide these data. However, this is a TGAI. There is no likelihood of oxidation/reduction potential for this chemical or any of the other components of the TGAI.

6. Flammability/Flame Extension (Guideline #830.6315; Required for a combustible liquid)

The registrant did not provide these data. The TGAI is not a combustible liquid. Data are not required.

7. Explodibility (Guideline #830.6316; Required if the product is potentially explosive)

The registrant did not provide these data. The TGAI powder is not potentially explosive. Data are not required.

8. Miscibility (Guideline #830.6319; Required if the product is an emulsifiable liquid and is to be diluted with petroleum solvents)

The registrant did not provide these data. The data are not required. The TGAI is a powder.

9. Corrosion Characteristics (Guideline #830.6320; Required)

The registrant did not provide these data. Data are not required for the TGAI.

10. Dielectric Breakdown Voltage (Guideline #830.6321; Required if the end product is a liquid and is to be used around electrical equipment)

The registrant did not provide these data. This is a TGAI and is not likely to be used around electrical equipment. Data are not required.

11. pH of Water Solutions or Suspensions (Guideline #830.7000; Required)

The pH was determined to be 5.16 (0.1% w/v dispersion in water).

12. UV/VIS Absorption (Guideline #830.7050; Required)

UV/VIS spectroscopy was performed for the test substance in methanol, acidic, neutral, and alkaline. The wavelengths of maximum absorbance are as follows: 281.4, 281.9, and 223.9 for acidic, neutral and alkaline conditions, respectively.

The data are adequate to support registration of the TGAI.

13. Viscosity (Guideline #830.7100; Required if the chemical is a liquid)

The registrant did not provide these data. The TGAI is a powder. Data are not required.

14. Melting Point/Melting Range (Guideline #830.7200; Required)

Examination of the differential scanning calorimetry endotherms with programmed heating indicated that melting starts at 252.3°C (525.5 K), with a peak at 253.4°C (526.6 K). No decomposition was observed at temperatures below 400°C.

The data are adequate to support registration of the TGAI.

15. Boiling Point/Boiling Range (Guideline #830.7220; Required if the TGAI is a liquid at room temperature)

The TGAI is a powder and these data are not required.

16. Density/Relative Density/Bulk Density (Guideline #830.7300; Required)

The relative density determined by a gas comparison pyknometer method was 1.714 with a standard deviation of 0.007.

The data are adequate to support registration of the TGAI.

17. Dissociation Constant in Water (Guideline #830.7370; Required)

The dissociation constant was determined by pH-metric titration to be pKa = 7.08 at 26°C.

The data are adequate to support registration of the TGAI.

18. Particle Size, Fiber Length and Diameter Distribution (Guideline #830.7520; Required)

The TGAI is not a fiber. The TGAI is a powder. These data are reviewed in conjunction with the toxicology inhalation data.

19. Partition Coefficient (n-Octanol/H_2O) (Guidelines #830.7550, 830.7560, 830.7570; Required)

The partition coefficient was log Pow = 3.5, within a 95% confidence range of 3.4 to3.6 as determined by HPLC simulation.

The data are adequate to support registration of the TGAI.

20. Water Solubility (Guideline #830.7840 Required)

Water solubility by column elution at 20°C was 0.17 mg/L in unadjusted water (nominal pH of 4.9) and 016 mg/L in seawater (nominal pH of 8.1).

The data are adequate to support registration of the TGAI registration.

21. Vapor Pressure (Guideline #830.7950; Required)

The vapor pressure was evaluated by the Knudsen Effusion Method and was determined to be 1.9 x 10^{-8} Pa at 20°C and 4.6 x 10^{-8} Pa at 25°C.

The data are adequate to support registration of the TGAI.

COMMENTS

The nine studies provided for the product chemistry DER included most of the information required by the Group A and B, Series 830 Guidelines. Ten characteristics of the test substance, required by the guidelines, were not provided in the Study Reports, including: (1) Description of Formulation Process, (2) Oxidation/Reduction: Chemical Incompatibility, (3) Flammability/Flame Extension, (4) Explodibility, (5) Miscibility, (6) Corrosion Characteristics, (7) Dielectric Breakdown Voltage, (8) Viscosity, (9) Boiling Point/Boiling Range, and (10) Particle Size, Fiber Length and Diameter Distribution and are not required for this TGAI powder.

BIBLIOGRAPHY

Cox, P. and D. Ristorcelli. (2001). "R107894: Determination of the Physico-Chemical Properties (pH, pKa, and EC Tests A4, A6, and A8)". MRID 456739-06

Doehner, R.F. and M.C. Hofman. (2001). Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303268: OPPTS 830.1600, 'Description of Materials Used to Produce Product' and OPPTS 830.1620, 'Description of Production Process'". MRID 456958-02C

Knapp, P.W. (2002). "Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303,268: OPPTS 830.1670, 'Description of the Formation of Impurities'". MRID 456739-01C

Millen, W.G. (2001). "Validation of HRGC Method M-3467.01 to Assay for CL 312264 and CL 322697 in the Technical Grade of AC 303268". MRID 456739-03C

Ristorcelli, D. (2001). "R107894: Determination of Physico-Chemical Properties". MRID 456739-07

Yang, H. (2000). "Validation of the Ion Chromatographic Method M-3417.01 to Assay for Triethylamine (TEA) in the CL 303268 Technical Grade Active Ingredient (TGAI)". MRID 456739-02C

Yang, H. (2001). "Validation of High Performance Liquid Chromatographic Method M-3397.03 to Assay for the Minor Components in CL 3030268 Technical Grade Active Ingredient". MRID 456739-04C

Yang, H. (2002). "Validation of the High Performance Liquid Chromatographic Method M-3498 to Assay for CL 303268 in the Technical Grade Active Ingredient (TGAI)". MRID 456739-05C

Yang, H. (2002). "Preliminary Analysis and Certification of Ingredient Limits for the Technical Grade of AC 303268". MRID 456958-01C

CONFIDENTIAL APPENDIX FOR AC 303268
(ID NO. 043813-ET)

Pages 195-199 *Manufacturing process information may be entitled to confidential treatment*

DECISION PKG. NO. 220066 SUBM. DUE DATE 9/18/03

SUBMISSION BAR CODE # 631626 REVIEWER Kleavy-Munk

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 432-ET PM 33 ACTION CODE 115

DESCRIPTOR Place Data Under Review **FQPA**___ **NFQPA**___

[ ] CHILD RESISTANT PACKAGING: [ ] REQUIRED [ ] NOT REQUIRED

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
03/07/03	03/12/03	03/19/03

METHOD OF SUPPORT

[ ] CITE-ALL [ ] SELECTIVE
[ ] NOT SUBMITTED [ ] N/A

FORMULATORS EXEMPTION

[ ] SUBMITTED [ ] NOT SUBMITTED
[ ] N/A

REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
EFFICACY				
ACUTE TOX.				
RASSB TOX.				
ENVIRON. FATE				
FISH/WILDLIFE				
OTHER: :				

STATUS

RESPONSE CODE 13 RESPONSE DATE AUG 26 2003

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

AUG 2 0 2003

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. William Goodwine
Janessen Pharmaceutica, Inc.
11215 Trenton-Harbourton Road
Titusville, NJ 08560

Subject: ECONEA Technical
EPA Registration Number 43813-ET
Your Submission Dated March 7th, 2003
EPA Received Date March 12th, 2003

The application referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act(FIFRA), as amended, is unacceptable for the following reasons:

Upon conducting a new chemical screen on the submitted materials for the intended use pattern and the following comments apply:

The draft labeling provided for the information mentioned above is incomplete. Specified formulator use directions covering the application methods/use rates/equipment were not cited on the label nor provided in the form of a technical bulletin. Detailed information on the industrial processes used, and any post-application tasks performed by the industrial workers using this MUP is needed to better characterize any potential occupational exposure concerns. Janessen Pharmaceutica, Inc. must provide detailed information on the industrial mixing/loading and application processes and any post-application worker(bystander) tasks anticipated when using MUP to formulate antifoulant paint end-use products(i.e., Sigma Nexxium 20 Antifouling). Refer to the following human exposure data guidelines to develop this needed information:

GLN 875.1700 and 875.2700 Product Use Information
GLN 875.2800 Description of Human Activity

Please Note: the precautionary statements for ECONEA product labeling must be revised according to FIFRA guidance for Toxicity Category I products which carry the DANGER signal word. Specifically, the addition of clear PPE statements for use of protective clothing and chemical-resistant gloves.

The findings of the actual review will not be complete without a full battery of toxicity data.

A complete copy of the science memo is enclosed for your records.

The product mentioned above has not passed the chemical screen, however, based upon our agreement to initiate a review of all submitted data, except toxicity data due to missing studies, data reviews are still progressing.

The Agency reserves a full label review until the above discrepancies have been clarified.

DP #: (289029)

Decision #: 220066

S631626

~~03-AUG-03~~

03-7-03

03-12-05

DATA PACKAGE BEAN SHEET

Date: 04-Aug-2003

* * * Registration Information * * *

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA

Risk Manager: RM 33 - Marshall - Swindell - (703) 308-6341 Room# CM-2 308H

Risk Manager Reviewer: Karen Leavy - KLEAVY

Sent Date: 19-Mar-2003 Calculated Due Date: 18-Sep-2003 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: NEW INGREDIENT;NEW REGISTRATION;NON-FOOD/FEED USE;

Ingredients: 119093

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 20-Mar-2003 Due Back:

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title:

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

Assigned To		Date In	Date Out	
Organization:	AD / RASSB	14-May-2003	04-Aug-2003	Administrative Due Date: 18-Jul-2003
Team Name:	RASSB2	14-May-2003	01-Aug-2003	Negotiated Due Date:
Reviewer Name:	Aviado, Doreen	14-May-2003	17-Jul-2003	Projected Completion Date:
Contractor Name:				

* * * Studies Sent for Review * * *

Printed on Page 2

* * * Additional Data Package for this Decision * * *

Printed on Page 3

* * * Data Package Instructions * * *

Please review new chemical human exposure data foracceptability.(DAVIADO)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

AUG - 4 2003

MEMORANDUM

SUBJECT: Review of Human Exposure Data in Support of Registration for **ECONEA ™ Technical** (EPA File Symbol 43813-ET), an antifoulant manufacturing-use product (MUP) containing 93.2 % of a new active ingredient (a.i.), **Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl).**

TO: Dennis Edwards, Chief
Marshall Swindell, Product Manager, Team 33
Regulatory Management Branch I
Antimicrobials Division (7510C)

FROM: Doreen Aviado, Biologist Doreen Aviado 7/17/03
Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

THRU: Nader Elkassabany, Team Leader NE 8/1/03
Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

Norm Cook, Chief 2 Y. Cook 8/4/03
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

DP Barcode: D289029 (Decision 220066)

Pesticide Chemical No.: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl) / 119093 (*R107894*, or AC 303268, CL 303268)

Registrant: Janssen Pharmaceutica Inc.

EPA File Symbol: 43813-ET

MRID No.: 456741-28

PURPOSE:

The Antimicrobials Division (AD), Product Management Team 33, requested a review for acceptability of the human exposure data submitted by the registrant, *Janssen Pharmaceutica Inc.*, in support of a registration application for **ECONEA ™ Technical** (EPA File Symbol 43813-ET), an MUP containing 93.2% of a new a.i., **Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)** (*R107894*, PC Code:119093) intended for use in formulating "anti-fouling products for control of hard fouling organisms". The Agency had conducted a "new chemical screen"in July, 2002 on portions of the submitted human exposure data. Additional information was provided to the Agency in a letter from the registrant dated September 26, 2002. These data have now been put into review.

Note that an occupational exposure assessment is reserved at this time for both primary handlers of the MUP and secondary handlers using formulated antifoulant paint EPs due to outstanding toxicology data issues impeding selection of appropriate toxicological endpoints needed for conducting an exposure/risk assessment. Issues exist regarding bridging of toxicity data from the parent compound "chlorfenapyr" to a "CL 303268" metabolite and the Agency has requested additional mammalian toxicity studies be conducted with the metabolite (T. McMahon, D286238, January 2, 2003).

BACKGROUND:

In support of registration for **ECONEA ™ Technical** MUP, as the a.i. technical source product for formulating antifoulant paint end products (EPs), *Janssen Pharmaceutica Inc.* provided data related to occupational exposure for the new active ingredient (a.i.), **Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)** (aka *R107894*). Data were screened for acceptability in addressing human exposure data needs as part of the "new chemical screen" process. A report on the findings from the July, 2002 screen is attached to this review as reference (D. Aviado, D284099, August 11, 2002). A letter from PM 33 was sent to the registrant August 14, 2002 covering the new chemical screen findings for each of the science disciplines, including the recommendations made in the human exposure screen for additional information to better characterize the product use applications and human activities involved. Specifically, the registrant was requested to provide :

- Detailed information on the industrial processes used (mixing/loading/application), and any post-application worker (bystander) tasks anticipated when using this MUP to formulate antifoulant paint end-use products. The registrant was encouraged to refer to the following human exposure data guidelines to develop this needed information:

  GLN 875.1700 and 875.2700 Product Use Information
  GLN 875.2800 Description of Human Activity

In response, the registrant sent a transmittal letter dated September 26, 2002 addressing the screen findings and the deficiencies cited by the Agency. This letter included requested human exposure information on the MUP covering the industrial formulation process for manufacturing

antifoulant paints from **ECONEA ™ Technical**.

In addition, human exposure data for handlers of the proposed antifoulant paint EPs were provided by *Janssen Pharmaceutica Inc.* in the form of an occupational exposure report (MRID 456741-28) dated January 11, 2002, entitled "*Screening Level Occupational Exposure Assessments For RI07894 (CL303268) As An Antifoulant In Paint Applied To Underwater Hulls*." This report supports the use pattern for the MUP, but is specifically intended for addressing human exposure data needs for the pending EP registration of **Sigma Nexxium 20 Antifouling** (EPA File Symbol 11350- GL), containing a co-biocide mixture of 3.4% of the new a.i. *RI07894* and 3.4% *Sea-Nine 211*. The submitted assessments are intended to qualitatively evaluate the potential worker exposures during shipyard painting operations and address, in a broad sense, the Human Exposure Data requirements under Series 875 Guidelines. As a conservative screening tool the assessment also includes quantitative dermal/inhalation exposure estimates and calculated MOEs for different painter scenarios (i.e., paint mixer/loader/applicator scenarios) based on surrogate data from PHED.

FINDINGS:

Human exposure data provided by *Janssen Pharmaceutica Inc.* on the industrial paint formulation process and the screening level assessments on occupational exposure (MRID 456741-28) are acceptable and satisfy data requirements under Series 875 Guidelines. The Agency will rely on these data in the future when conducting an exposure/risk assessment in support of registration of **ECONEA ™ Technical** MUP and the pending **Sigma Nexxium 20 Antifouling** EP registration.

cc: Doreen Aviado AD/RASSB
Chemical File
Circulation File

Attachment

SUBJECT: Input for the *7/24/02 New Chemical Screen Meeting* on a new active ingredient (a.i.), **Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)**, proposed for use as an antifoulant preservative. Occupational exposure considerations regarding the *Janssen Pharmaceutica Inc.* registration application for the 93.2 % a.i. manufacturing-use product (MUP): **ECONEA ™ Technical** (EPA File Symbol 43813-ET); and Human Exposure Data requirements for the *Sigma Coatings USA* registration application for the 3.4 % a.i. end-use product (EP): **Sigma Nexxium 20 Antifouling** (EPA File Symbol 11350-GL) which also contains 3.4 % *Sea-Nine 211* as an a.i. co-biocide.

TO: Norm Cook, Chief
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

FROM: Doreen Aviado, Biologist
Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

THRU: Nader Elkassabany, Team Leader
Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

DP Barcode: D284099 (S617867)

Pesticide Chemical(s)/ No.(s): MUP: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl) / 119093 (*R107894*, or AC 303268, CL 303268)

EP: 2-(p-chlorophenyl)-3-cyano- 4-bromo-5-triflouromethylpyrolle /119093 and 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one / 128101 (*Sea-Nine 211*, or C-9211, RH-287, or Kathon 287T)

MRID No.: 456741-28

PURPOSE:

The purpose for conducting this "new chemical screen" is three-fold:

1) To conduct a new chemical screen of materials provided by the registrant, *Janssen Pharmaceutica Inc.*, to Product Management Team 33 (PM 33) in support of a registration application for **ECONEA ™ Technical** (EPA File Symbol 43813-ET), an MUP containing 93.2% of a new a.i., **Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)**

(*R107894*, PC Code:119093) intended for use in formulating "anti-fouling products for control of hard fouling organisms"; and

2) To conduct a new chemical screen of materials jointly submitted by *Janssen Pharmaceutica Inc.* and the EP registrant, *Sigma Coatings USA*, to PM 33 in support of a registration application for the formulated paint product, **Sigma Nexxium 20 Antifouling** (EPA File Symbol 11350- GL), containing a co-biocide mixture of 3.4% of the new a.i. *R107894* and 3.4% *Sea-Nine 211*; also

3) To decide if enough data have been provided in the registrants' submissions to facilitate putting the packages into RASSB review for assessing any applicable Human Exposure Data requirements needing to be addressed.

BACKGROUND:

In support of registration for **ECONEA ™ Technical** MUP, as the a.i. technical source product, and the formulated **Sigma Nexxium 20 Antifouling** paint EP, *Janssen Pharmaceutica Inc.* and *Sigma Coatings USA* provided administrative materials including transmittal letters, product labeling and CSFs, meeting minutes, and data matrices citing studies conducted in support of the new active ingredient (a.i.), **Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)** (aka *R107894*), as an alternative to TBTO in formulating antifoulant coatings.

Prior to submission of the registration applications, representatives of *BASF Corporation* (the a.i. manufacturer), *Janssen Pharmaceutica Inc.* (intended registrant of the technical source MUP), and *Sigma Coatings USA* (intended registrant of the formulated antifoulant paint EP) met with the Agency March 7, 2001 for a pre-application meeting to discuss data requirements for both the MUP and EP. Minutes from that meeting dated May 20, 2001 outline the following regarding human exposure data issues:

- Agency requested application/post-application information (data) in the form of a technical bulletin, product use information (MUP and EP), and description of human activities;

- "AD discussed possible submission of a 'human health exposure risk assessment' in lieu of conducting a dermal/inhalation exposure monitoring study once the Agency has reviewed the toxicity data and established toxicological endpoints."

Human exposure data were provided by *Janssen Pharmaceutica Inc.* in the form of an occupational exposure report (MRID 456741-28) dated January 11, 2002, entitled "*Screening Level Occupational Exposure Assessments For R107894 (CL303268) As An Antifoulant In Paint Applied To Underwater Hulls.*" This report supports the formulated **Sigma Nexxium 20 Antifouling** EP and appears to address potential occupational exposure concerns the Agency discussed with the registrants' in the March 7, 2001 pre-application meeting. The submitted assessments are intended to qualitatively evaluate the potential worker exposures during shipyard painting operations and address, in a broad sense, the Human Exposure Data requirements under Series 875 Guidelines. As a conservative screening tool the assessment also includes quantitative dermal/inhalation exposure estimates and calculated MOEs for different painter scenarios (i.e., paint mixer/loader/applicator scenarios) based on surrogate data from PHED.

NON-FQPA

DP BARCODE: D290345

CASE: 072289 DATA PACKAGE RECORD DATE: 05/28/03
SUBMISSION: S636241 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REGISTRATION ACTION: 116 RESB NC-NON-FOOD/FEED U
CHEMICALS: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)- 99.0000%

ID#: 043813-ET ECONEA TECHNICAL
COMPANY: 043813 JANSSEN PHARMACEUTICA
PRODUCT MANAGER: 33 MARSHALL SWINDELL 703-308-6341 ROOM: CS1 6B
PM TEAM REVIEWER: KAREN LEAVY-MUNK 703-308-6237 ROOM: CS1 6W9
RECEIVED DATE: 03/28/03 DUE OUT DATE: 10/04/03

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 290345 EXPEDITE: N DATE SENT: 05/28/03 DATE RET.: / /
CHEMICAL: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)-5-(triflu
P TYPE: 001
CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT	ADMIN DUE DATE: 09/25/03
DIV : AD	/ /	/ /	NEGOT DATE: / /
BRAN: RASSB	/ /	/ /	PROJ DATE: / /
SECT: RASSB1	/ /	/ /	
REVR :	/ /	/ /	
CONTR:	/ /	/ /	

* * * DATA REVIEW INSTRUCTIONS * * *

Please review the the attached data (MRID's 458939-01; -02; -03; -04; -05; and -07) for acceptability.

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL

NON-EUPA

SUBMISSION BAR CODE # 5436239 REVIEWER Kleung-Mu h K

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 43813-ET PM 33 ACTION CODE 116

DESCRIPTOR Support Data

[ ] CHILD RESISTANT PACKAGING: [ ] CERTIFICATION
[ ] NON-RESIDENTIAL USE ONLY
[ ] NOT APPLICABLE

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL

PROPOSED CLASSIFICATION: [ ] GENERAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
03 27 03	03 28 03	03 31 03

~~METHOD OF SUPPORT~~

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[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

FORMULATORS EXEMPTION

[ ] SUBMITTED
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
EFFICACY				
TOXICOLOGY				
HED TOX.				
ENVIRON. FATE				
FISH/WILDLIFE				
OTHER				

STATUS

RESPONSE CODE 10 RESPONSE DATE MAY 27 2003

APR - 7 2003

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

JANSSEN PHARM. RESEARCH FOUNDATION
P.O. BOX 200
1125 TRENTON-HARBOURTON ROAD
TITUSVILLE, NJ 085600200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 03/28/03. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents. If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below. These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels. The rejected studies and their deficiencies are described below.

Rejected study [06] :

* Judging from the pagination of the study, pages. . . 51. . were omitted from the submitted copy.

JANSSEN PHARMACEUTICA INC.

458939-00

March 27, 2003

Document Processing Desk
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

ATTN: Mr. Marshall Swindell - Product Manager, Team 33
Antimicrobial Division (7510W)
Regulatory Management Branch II

SUBJECT: ECONEA™ Technical (Janssen Code No. R107894)
Supplementary Data Submission
EPA File Symbol: 43813-ET

Dear Mr. Swindell:

Janssen Pharmaceutica Inc. is making a supplementary data submission for the registration of ECONEA™ Technical for formulation of antifouling treatment products under the general use pattern of aquatic non-crop. Your letter of 18 March 2003 indicates that the ECONEA submission, including ecological effects data, will be placed into formal review.

The ECONEA Technical application for registration is linked to the end-use antifouling paint product, NEXXIUM™ 20, from Sigma Coatings with EPA file symbol 11350-GL.

Three (3) copies each of the following reports, and an updated Data Support Matrix are enclosed.

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TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000

us.janssen.com

ECO-TOXICITY (40 CFR Part 158.490)

Parent Compound R107894

Volume 1 R107894 – Early Life-Stage Toxicity Test with Zebra Fish *(Danio rerio)*, Springborn-Smithers Laboratories Report No. 13751.6132, (Janssen Rpt. No. AGR 533), March 14, 2003, OPPTS Draft Guideline 850.1400.

MRID 45893901

Volume 2 R107894 – Toxicity to the Freshwater Blue-Green Alga, *Anabaena flos-aquae*, Springborn-Smithers Laboratories Report No. 13751.6137, (Janssen Rpt. No. AGR 398), February 10, 2003, OPPTS Draft Guideline 850.5400.

MRID 45893902

Volume 3 R107894 – Toxicity to the Freshwater Diatom, Navicula pelliculosa, Springborn-Smithers Laboratories Report No. 13751.6133, (Janssen Rpt. No. AGR 391), January 28, 2003, OPPTS Draft Guideline 850.5400.

MRID 45893903

Metabolite CL 322,248

Volume 4 CL 322,248 – Toxicity to the Freshwater Blue-Green Alga, *Anabaena flos-aquae*, Springborn-Smithers Laboratories Report No. 13751.6139, (Janssen Rpt. No. AGR 478), March 14, 2003, OPPTS Draft Guideline 850.5400.

MRID 45893904

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Volume 5 CL 322,248 – Toxicity to the Freshwater Diatom, *Navicula pelliculosa,* Springborn-Smithers Laboratories Report No. 13751.6135, (Janssen Rpt. No. AGR 479), March 17, 2003, OPPTS Draft Guideline 850.5400.

MRID 45893905

Metabolite CL 325,195

Volume 6 CL 325,195 – Toxicity to the Freshwater Blue-Green Alga, *Anabaena flos-aquae*, Springborn-Smithers Laboratories Report No. 13751.6140 (Janssen Rpt. No. 388), February 10, 2003, OPPTS Draft Guideline 850.5400.

MRID REJ(06)

Volume 7 CL 325,195 – Toxicity to the Freshwater Diatom, *Navicula pelliculosa*, Springborn-Smithers Laboratories Report No. 13751.6136 (Janssen Rpt. No. 393), January 29, 2003 OPPTS Draft Guideline 850.5400.

MRID 45893906

Metabolite CL 322,250

Volume 8 CL 322,250 – Toxicity to the Freshwater Blue-Green Alga, *Anabaena flos-aquae*, Springborn-Smithers Laboratories Report No. 13751.6138 (Janssen Rpt. No. 389), February 19, 2003, OPPTS Draft Guideline 850.5400.

MRID 45893907

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JANSSEN PHARMACEUTICA INC.

Volume 9 CL 322,250 – Toxicity to the Freshwater Diatom, *Navicula pelliculosa*, Springborn-Smithers Laboratories Report No. 13751.6134 (Janssen Rpt. No. 392), February 17, 2003, OPPTS Draft Guideline 850.5400.

MRID 45893908

Please contact me directly on any matters relating to this registration application.

Sincerely,

Bill Goodwine

William R. Goodwine
Senior Director
Plant & Material Protection Division
Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwi@janus.jnj.com

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CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 4813-ET PM 33 ACTION CODE 116

DESCRIPTOR Data Matrix

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DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
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METHOD OF SUPPORT

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FORMULATORS EXEMPTION

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REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
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TOXICOLOGY				
HED TOX.				
ENVIRON. FATE				
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DATA MATRIX

Date April 22, 2002	EPA Reg No./File Symbol 43813	Page 8 of 16
Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Eco-Toxicity - Parent Compound R107894

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.1075	Fish acute toxicity test, freshwater Rainbow Trout		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1075	Fish acute toxicity test, freshwater Bluegill		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1075	Fish acute toxicity test, marine		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1010	Aquatic invertebrate acute tox, test, freshwater daphnids		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1025	Oyster acute toxicity test (shell deposition)		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1035	Mysid acute toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1400	Fish early-life stage toxicity test - marine		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1300	Daphnid chronic toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1350	Mysid chronic toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1735	Whole sediment acute toxicity invertebrates, freshwater		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1740	Whole sediment acute toxicity invertebrates, marine		Janssen Pharmaceutica Inc.	OWN	
Guideline 71-1(a)	Avian single dose LD50 test - Mallard Duck	43492808	BASF	EXC	
Guideline 71-1(a)	Avian single dose LD50 test - Bobwhite Quail	43492809	BASF	EXC	
OPPTS Guideline 850-1400	Fish early-life stage toxicity test - Freshwater		Janssen Pharmaceutica Inc.	OWN	

Signature William R. Goodwine	Name and Title William R. Goodwine	Date March 26, 2003

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version. Agency Internal Use Copy

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DATA MATRIX

Date April 22, 2002	EPA Reg No./File Symbol 43813	Page 12 of 16
Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Plant Protection/Non-Target Plants/Parent Compound R107894

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.4100/4225	Terrestrial plant toxicity, Tier 1 (seedling emergence)		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.4400	Aquatic plant tox test using Lemna spp. Tiers I and II		Janssen Pharmaceutica, Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Raphidocelis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Skeletonema		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Freshwater Blue-green		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Freshwater Diatoms		Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	3/26/03 ~~April 22, 2002~~

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DATA MATRIX

Date April 22, 2002	EPA Reg No./File Symbol 43813	Page 13of 16
Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Plant Protection/Non-Target Plants/Metabolite CL 325, 195

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.4400	Aquatic plant tox test using Lemna spp. Tiers I and II		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Raphidocelis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Skeletonema		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Freshwater Blue-green		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Freshwater Diatoms		Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	3/26/03 ~~April 23, 2002~~

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DATA MATRIX

Date April 22, 2002	EPA Reg No./File Symbol 438 f3	Page 15 of 16
Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	
Ingredient R107894	Plant Protection/Non-Target Plants/Metabolite CL 322,248	

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.4400	Aquatic plant tox test using Lemna spp. Tiers I and II		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Raphidocelis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Skeletonema		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Freshwater Blue-green		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Freshwater Diatoms		Janssen Pharmaceutica Inc.	OWN	

Signature William R. Goodwine	Name and Title William R. Goodwine	Date 3/24/03 ~~April 22, 2002~~

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SUBMISSION BAR CODE # S62357B REVIEWER T. McMahon

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 4313-ET PM 33 ACTION CODE 011

DESCRIPTOR ECONEA Technical

[ ] CHILD RESISTANT PACKAGING: [ ] CERTIFICATION
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[ ] NOT APPLICABLE

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL

PROPOSED CLASSIFICATION: [ ] GENERAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
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METHOD OF SUPPORT:
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FORMULATORS EXEMPTION
[ ] SUBMITTED
[ ] NOT SUBMITTED
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REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
EFFICACY				
TOXICOLOGY				
HED TOX.				
ENVIRON. FATE				
FISH/WILDLIFE				
OTHER _____				

STATUS _____

RESPONSE CODE 9 RESPONSE DATE 01/09/03

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

JAN 09 2003

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr.Bill Goodwine
Janssen Pharmaceutica, Inc.
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

Subject: ECONEA Technical
EPA File Symbol 43813-ET
Your Submission Dated September 30th, 2002
EPA Received Date October 3rd, 2002

The submission referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, as per your rebuttal letter regarding the bridging of toxicology data for chlorfenapyr to the metabolite, CL303268, to support the registration of CL 303268 as an active ingredient in the antifouling paint product, "Sigma Nexxium 20 Antifouling and the technical material (ECONEA antifouling preservative), is unacceptable.

Upon review of the bridging toxicology data for the parent compound chlorfenapyr to address the toxicity of the CL303268 metabolite, the Agency has determined that it is incomplete. There is not enough submitted toxicity data for the CL 303268 metabolite to establish whether there is any concordance in toxicity between the parent, chlorfenapyr, and the metabolite(CL303268).

The proposed mode of action for the CL303268 metabolite is NOT entirely reflective of the toxicity of chlorfenapyr. Since there is a lack of concordance in the toxicity between chlorfenapyr and CL303268 metabolite and lack of data for two compounds demonstrating any concordance, the Agency has determined that the submitted toxicity database for chlorfenapyr does not support the registration of the CL 303268 metabolite.

Therefore, the Agency requests the submission of the following studies, a 90-day oral toxicity with neurotoxicity endpoints included in the study design, a developmental toxicity study in a rat, and a mutagenicity study battery, to better establish the relationship of the CL 303268 metabolite to chlorfenapyr.

The findings of the actual review will not be complete without a full battery of toxicity data.

A complete copy of all the science memos are enclosed for your records

The product mentioned above has failed the new chemical screen. The data will not be put into review until the above discrepancies have been clarified.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,

Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

MAR 18 2003

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr.Bill Goodwine
Janssen Pharmaceutica, Inc.
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

Subject: ECONEA Technical
EPA File Symbol 43813-ET
Agreement to Generate Bridging Data

Dear Mr. Goodwine:

This will acknowledge your recent letter of in which you commit to conducting the following toxicology studies:

-90-day oral in rat with neuropathology evaluation (via perfusion fixation of central and peripheral nervous system)

-Development toxicity study in the rat

-Mammalian cell CHO/HGPRT mutagenicity Study

- In vivo mouse micronucleus test

As agreed upon in the meeting, because of the unusual circumstances associated with this new active ingredient, the Agency will place the environmental and ecological effects data as well as the chemistry and end-use application into review in the absence of a complete data package. Normally a new active ingredient submission must be a complete package before the Agency will start its review process. Please note that when the toxicology data are submitted they will be placed into review on a track independent of the environmental and other reviews.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,

Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN - 2 2003

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM December 20, 2002

SUBJECT: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(triflouromethyl)-; CL 303268: Response to the registrant's rebuttal to toxicology issues raised from the New Chemical Screen of CL 303268.

EPA Identification Numbers:

P.C. Codes: 119093

MRID's: N/A (correspondence)
DP Barcode: D286238

TO: Marshall Swindell/Karen Leavy-Munk
Regulatory Management Branch II / PM Team 33
Antimicrobials Division (7510C)

FROM: Timothy F. McMahon, Ph.D. 12/20/02
Senior Toxicologist
Antimicrobials Division (7510C)

THRU: Nader Elkassabany, Ph.D. NE 12/20/02
Team Leader, Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

and

Norm Cook, Chief 01.02.03
RASSB
Antimicrobials Division (7510C)

Action Requested: Respond to the registrant's rebuttal regarding bridging of toxicology data for chlorfenapyr to the chlorfenapyr metabolite CL 303268 to support the registration of CL 303268 as an active ingredient in the antifouling paint product Sigma Nexxium 20 Antifouling, and the technical material (Econea antifouling preservative). .

Background

Janssen Phamaceutical, Titusville, New Jersey, previously submitted applications to the Environmental Protection Agency for registration of the manufacturing-use product ECONEA technical (containing 93.2% CL 303268 as active) and the formulated product Sigma Nexxium 20 Antifouling (containing CL 303268 at 3.4% and C9-211 at 3.4%)

The registrant put forth the proposal that toxicology data for the parent compound chlorfenapyr could be bridged to address toxicity of the CL 393268 metabolite. The registrant used several lines of argument. As stated in the previous memo and repeated here for continuity, the primary argument is that the mode of action of chlorfenapyr can be attributed to the CL 303268 metabolite (from page 11 of the submitted discussion: " the insecticidal activity of parent chlorfenapyr can be attributed to CL 303268. CL 303268 was shown to be an extremely potent insecticide with LC50 values of < 10 ppm against southern armyworms and tobacco budworms. In addition, the mammalian toxicity of chlorfenapyr can be attributed to CL 303268, as CL 303268 was shown to be highly toxic to mammals by the acute oral route.") [Note: This claim is based on the following: the LC50 value of the CL 303268 metabolite is very low, i.e. < 10ppm. also, the acute oral toxicity of this metabolite is lower (27-29 mg/kg/day) vs. the parent (441(M) and 1152 (F) mg/kg/day)].

In response to the registrant's submission, the Antimicrobials Division pointed out (in memorandum D284098) that the mode of action for chlorfenapyr had never been previously submitted to the Agency for review, and that arguments supporting the CL 303268 metabolite as the proximate species responsible for the insecticidal activity of chlorfenapyr would have to be examined by the Agency.

Discussion

Chlorfenapyr is registered with the Office of Pesticide Programs as an agricultural use pesticide. Specifically, chlorfenapyr is an insecticide-miticide for use on cotton, vegetables, citrus and ornamentals A temporary tolerance has been established in/on cottonseed at 0.5 ppm (PP#5F04456). Temporary tolerances of 0.5 ppm have also been proposed for oranges and lemons (PP#5G04507).

The registrant submitted additional data in support of the conclusion that the CL 303268 metabolite is an uncoupler of oxidative phosphorylation (Black, B.C. et al., *Insecticidal Action*

and Mitochondrial Uncoupling Activity of AC-303,630 and Related Halogenated Pyrroles, Pesticide Biochemistry and Physiology Vol. 50: pp. 115-128, 1994; Hunt, D.A. and Treacy, M.F.: Pyrrole Insecticides: A New Class of Agriculturally Important Insecticides Functioning as Uncouplers of Oxidative Phosphorylation; In Ishaaya I. and D. Degheele (eds.), Insecticides with novel modes of action: mechanism and application, Springer-Verlag, New York, Berlin, Chapter 8, pages 139-151, 1997; Gange, D.M., et al., The QSAR of Insecticidal uncouplers. In Hansch, C. and T. Fujita (eds.). Classical and three-dimension QSAR in agrochemistry, American Chemical Society, Chapter 15: pages 199-212, 1995). These data do appear to support the argument that CL 303268 does possess this property.

Examination of the toxicity database for chlorfenapyr shows that the liver is a target organ of toxicity for chlorfenapyr. In the 28-day dermal toxicity study in the rabbit and in carcinogenicity studies in the rat, the primary toxic effects observed were in the liver (increased cholesterol, increased liver weight and cytoplasmic vacuolation in the 28-day study; hepatocellular adenoma in male rats in the carcinogenicity study in rats). In addition, a one-year neurotoxicity study in rats and a chronic toxicity/carcinogenicity study in mice showed significant nervous system toxicity, including vacuolation of the central nervous system (brain, spinal cord, optic nerve). The toxicity of chorfenapyr to the liver is not likely related to the proposed mechanism of action, i.e. uncoupling of oxidative phosphoryation, but some other mechanism. The central nervous system toxicity on the other hand could be possibly related to the uncoupling effect. As noted in Chapter 16 of Casarett and Doulls' Fifth Edition of Toxicology: The Basic Science of Poisons (1996), " Neurons are highly dependent upon aerobic metabolism for energy requirements. Cells of the nervous system must be able to produce large quantities of high energy phosphates even at rest to meet the demand for maintenance and repetitive reinstitution of ion gradients necessary for membrane depolarization and repolarization." "The systemic exposure to toxicants that inhibit aerobic respiration, such as cyanide...leads to the earliest signs of dysfunction in the myocardium and neurons." Thus, even a brief interruption in the energy supply to neurons will be detrimental, as the nervous system is more sensitive to the effects of oxidative phosphorylation uncoupling than other systems in the body.

There is not enough submitted toxicity data for the CL 303268 metabolite to establish whether there is any concordance in toxicity between parent chlorfenapyr and the CL 303268 metabolite. The proposed mode of action for the CL 303268 metabolite is not entirely reflective of the toxicity of chlorfenapyr. There are likely differences in the dose-response for toxicity between the parent chlofenapyr and the CL 303268 metabolite, which is partially evident when comparing the acute oral LD50 values between the two compounds as noted above.

Conclusions

The lack of concordance in the toxicity between chlofenapyr and the CL 303268 metabolite and the lack of data for the two compounds demonstrating any concordance does not support using the toxicity database for chlofenapyr to support registration of the CL 303268 metabolite. In addition, the signs of neurotoxicity produced in long-term studies with chlorfenapyr needs to be investigated further with respect to the CL 303268 metabolite, as this metabolite, through the uncoupling mechanism, may have some relationship to the neurotoxic effects observed with chlorfenapyr. If the CL 303268 metabolite is in fact the proximal toxicant, its neurotoxicity might even be higher than that of the parent. It is very possible that the toxicity of the CL 303268 metabolite is different than the toxicity of parent chlorfenapyr from the available data. Neurotoxic effects are of particular concern.

In order to better establish the relationship of the CL 303268 metabolite to chlorfenapyr, the registrant will need to conduct the following studies with the CL 303268 metabolite: a 90-day oral toxicity study with neurotoxicity endpoints included in the study design, a developmental toxicity study in the rat, and a mutagenicity testing battery (the registrant appears to already have an Ames assay, but needs to complete the testing battery with two other studies). In this way, the toxicity of the parent chlorfenapyr realtive to CL 303268 metaoblite can be assessed and a decision can be made as to whether these studies are adequate to bridge toxicity data from the parent for this metabolite.

DP BARCODE: D286238

CASE: 072289 DATA PACKAGE RECORD DATE: 01/03/03
SUBMISSION: S623573 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REGISTRATION ACTION: 011 RESUB NEW CHEM SCRNG
CHEMICALS: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)- 99.0000%

ID#: 043813-ET ECONEA TECHNICAL
COMPANY: 043813 JANSSEN PHARMACEUTICA
PRODUCT MANAGER: 33 MARSHALL SWINDELL 703-308-6341 ROOM: CS1 6B
PM TEAM REVIEWER: KAREN LEAVY-MUNK 703-308-6237 ROOM: CS1 6W9
RECEIVED DATE: 10/03/02 DUE OUT DATE: 01/01/03

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 286238 EXPEDITE: Y DATE SENT: 10/18/02 DATE RET.: 01/02/03
CHEMICAL: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)-5-(triflu
DP TYPE: 001
CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT	ADMIN DUE DATE: 11/17/02
DIV : AD	10/18/02	01/02/03	NEGOT DATE: / /
BRAN: RASSB	10/18/02	01/02/03	PROJ DATE: / /
SECT: RASSB2	10/18/02	12/20/02	
REVR : TMCMAHON	10/23/02	12/20/02	
CONTR:	/ /	/ /	

* * * DATA REVIEW INSTRUCTIONS * * *

Norm this was sent through RASSB for tracking purposes and so that you would be aware of what's going on.
Please forward this rebuttal to AD's screening of the ECONEA antifoulant new chem tox comments. Please forward to Tim for review. Tim indicated that he will work on it and confer with HED. When done we will schedule a meeting with the company. Thanks, Karen Leavy/Swindell
If any additional information is needed please contact Karen (308-6237).

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL

Tim McMahon
07/25/2002 09:59 AM

To: Dennis Edwards/DC/USEPA/US@EPA, Norm Cook/DC/USEPA/US, Karen Leavy/DC/USEPA/US@EPA, Marshall Swindell/DC/USEPA/US@EPA
cc: Doreen Aviado/DC/USEPA/US
Subject: new chemical screen for ECONEA Technical

Dennis,

I met with Alberto Protzel of HED yesterday to discuss my concerns regarding the screen for ECONEA technical.

Alberto is a member of the Mechanism of Action Committee in HED and is also a member of the Metabolism Committee.

The company desires to bridge all of the toxicology data for chlorfenapyr to assess risks from the metabolite CL 303268 for use in antifoulant boat paint.

The company claims that the insecticidal action of chlorfenapyr is due to uncoupling of oxidative phosphorylation by the CL 303268 metabolite of chlorfenapyr and that the toxicology data for chlorfenapyr can be used to support hazard idenfication for the metabolite. Based on my discussion yesterday, there are issues that need to be addressed by the company prior to any consideration of their request.

1) There is no submitted data by the company that the CL 303268 metabolite is actually insecticidal by the proposed mode of action.

2) There is no submitted data that this metabolite ALONE is responsible for this mode of action (there are at least 5 metabolites of chlofenapyr in mammalian studies submitted so far) or that other modes of action may not be operative as well.

3) There is no proof that any of the other metabolites of chlorfenapyr may or may not also work by this mode of action.

4) The disposition of the CL 303268 metabolite may be quite different when administered directly compared to disposition of this metabolite when parent chemical is administered. The spectrum of toxicity of the metabolite may thus also be different.

5) Conduct of an acute oral toxicity study and a preliminary 28 day toxicity study with the CL 303268 metabolite is insufficient to make any claims supporting the mode of action

Normally, to support toxicity claims between a parent chemical and a metabolite of that chemical , bridging data are submitted as one aspect of the data needed. The Office of Pesticide Programs requests a 90-day oral toxicity study, a developmental toxicity study, and at least one mutagenicity study as bridging data. These studies must be conducted according to the OPPTS harmonized test guidelines, Series 870. These data are necessary to determine if the spectrum of toxicity is the same between the parent chemical and the metabolite and to get a reasonable idea of the relative potency of the toxicity of the compounds.

In addition, the company must support the claim that the insecticidal action of chlorfenapyr is through the action of the CL 303268 metabolite, and that this insecticidal action is by uncoupling of oxidative phosphorylation. These data will be reviewed by the Health Effects Division's Mechanism of Action Committee to determine if the data support the company's claim.

Although I am happy to provide this information for you I was a little surprised that it was needed in such a short time frame.

Tim McMahon
10/28/2002 11:14 AM

To: Karen Leavy/DC/USEPA/US@EPA
cc:
Subject: Re: Status of the science review for Janssen unregistered a.i. {43813-ET}

Karen,

You need to talk to Marshall about this. The tox issue needs to undergo peer review by scientists in AD and HED prior to any decision on the company's argument. Just to inform you, here is an earlier email that I wrote summarizing the problem with their submission:

"The company desires to bridge all of the toxicology data for chlorfenapyr to assess risks from the metabolite CL 303268 for use in antifoulant boat paint.

The company claims that the insecticidal action of chlorfenapyr is due to uncoupling of oxidative phosphorylation by the CL 303268 metabolite of chlorfenapyr and that the toxicology data for chlorfenapyr can be used to support hazard idenfication for the metabolite. There are issues that need to be addressed by the company prior to any consideration of their request.

1) There is no submitted data by the company that the CL 303288 metabolite is actually insecticidal by the proposed mode of action.

2) There is no submitted data that this metabolite ALONE is responsible for this mode of action (there are at least 5 metabolites of chlofenapyr in mammalian studies submitted so far) or that other modes of action may not be operative as well.

3) There is no proof that any of the other metabolites of chlorfenapyr may or may not also work by this mode of action.

4) The disposition of the CL 303268 metabolite may be quite different when administered directly compared to disposition of this metabolite when parent chemical is administered. The spectrum of toxicity of the metabolite may thus also be different.

5) Conduct of en acute oral toxicity study and a preliminary 28 day toxicity study with the CL 303268 metabolite is insufficient to make any claims supporting the mode of action

Normally, to support toxicity claims between a parent chemical and a metabolite of that chemical , bridging data are submitted as one aspect of the data needed. The Office of Pesticide Programs requests a 90-day oral toxicity study, a developmental toxicity study, and at least one mutagenicity study as bridging data. These studies must be conducted according to the OPPTS harmonized test guidelines, Series 870. These data are necessary to determine if the spectrum of toxicity is the same between the parent chemical and the metabolite and to get a reasonable idea of the relative potency of the toxicity of the compounds.

In addition, the company must support the claim that the insecticidal action of chlorfenapyr is through the action of the CL 303268 metabolite, and that this insecticidal action is by uncoupling of oxidative phosphorylation. These data will be reviewed by the Health Effects Division's Mechanism of Action Committee to determine if the data support the company's claim.

Karen Leavy

Karen Leavy
10/28/02 10:39 AM

To: Tim McMahon/DC/USEPA/US@EPA
cc:
Subject: Status of the science review for Janssen unregistered a.i. {43813-ET}

Tim,

Can you give me a status on the pending sceince review for the unregistered a.i. 43813-ET? The DP barcode
for this submission is D286238.

Thanks,

KML

PRECAUTIONARY STATEMENT
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

DANGER

Fatal if swallowed. Corrosive. Causes irreversible eye damage. Do not get in eyes or on clothing. Wear protective eyewear such as goggles, face shield or safety glasses. Wash thoroughly with soap and water after handling and before eating, drinking, or using tobacco. Harmful if inhaled or absorbed through the skin. Avoid breathing dust. Avoid contact with skin, eyes, or clothing. Remove contaminated clothing and wash clothing before reuse.

FIRST AID	
If swallowed	-Call a poison control center or doctor immediately for treatment advice. -Have person sip a glass of water if able to swallow. -Do not induce vomiting unless told to do so by a poison control center or doctor. -Do not give anything by mouth to an unconscious person.
If in eyes	-Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. -Call a poison control center or doctor for treatment advice.
If inhaled	-Move person to fresh air. -If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. -Call a poison control center or doctor for further treatment advice
If on skin or clothing	-Take off contaminated clothing. -Rinse skin immediately with plenty of water for 15-20 minutes. -Call a poison control center or doctor for treatment advice.
HOT LINE NUMBER: Chem Trec: (800) 424-9300 Have the product container with you when calling a poison control center or doctor, or going for treatment	
NOTE TO PHYSICIAN Probable mucosal damage may contraindicate the use of gastric lavage.	

ECONEA™

Technical

Anti-fouling Preservative

For Formulating Use Only

ACTIVE INGREDIENT: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)	93.2%
INERT INGREDIENTS:	6.8%
TOTAL:	100.0%

KEEP OUT OF REACH OF CHILDREN

DANGER **POISON**

See side panel for first aid and additional precautionary statements.

EPA Reg. No.:43813-XX
EPA Est. No.: 241-MO-001

NET Contents: 110 lbs. (50 kgs)

JANSSEN PHARMACEUTICA
1125 Trenton-Harbourton Road
Titusville, NJ 08560

04/02

DIRECTIONS FOR USE
It is a violation of Federal law to use this product in a manner inconsistent with its labeling.
This product is for formulation into anti-fouling products for control of hard fouling organisms. Each formulator is responsible for obtaining EPA registration for their end-use product(s).

STORAGE AND DISPOSAL
PROHIBITIONS: Do not contaminate water, food or feed by storage and disposal.
STORAGE: DO NOT mix or store this product or solutions of this product in a manner inconsistent with its labeling.
DISPOSAL: Pesticide wastes may be acutely hazardous. Improper disposal is a violation of Federal Law.
PESTICIDE DISPOSAL: Pesticide, mixtures, or equipment rinse waters that cannot be chemically reprocessed must be disposed of according to applicable federal, state or local procedures. Contact your State Pesticide or Environmental Control Agency or the Hazardous Waste representative at the nearest EPA Regional Office for guidance.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into formulation equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If burned, stay out of smoke. If drum is contaminated and cannot be reused, dispose of in the same manner.

ENVIRONMENTAL HAZARDS
Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

NOTICE OF WARRANTY
Janssen Pharmaceutica warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with the directions under normal use conditions. It is impossible to eliminate all risks inherently associated with the use of this product. Ineffectiveness or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of Janssen Pharmaceutica. In no case shall Janssen Pharmaceutica be liable for consequential, special or indirect damages resulting from the use or handling of this product. The Buyer shall assume all such risks. Janssen Pharmaceutica makes no warranties of merchantability of fitness for a particular purpose or any other express or implied warranty except as stated above.

JANSSEN PHARMACEUTICA INC.

Proposed Agenda for ECONEA™ Antifouling Agent

Attendees:

JANSSEN:	Bill Goodwine	Senior Director, US
	Piet Blancquaert	Senior Manager, Belgium
BASF:	Jack Arthur	Manager, Global Regulatory Affairs
	Ada Breaux	Washington Representative
SIGMA:	Mike Winter	Technical Manager
NAVSEA:	Dr. Alexis Kaznoff	Director, SEA 05M, Materials & Environment
	Mark Ingle, P.E.	Project Mgr, Antifouling Coatings
EPA – AD:	(requested)	
	Frank Sanders	AD Division Director
	Jack Housenger	AD Associate Division Director
	Dennis Edwards	AD Branch Chief I
	Marshall Swindell	PM 33, Antifouling

Focus for Discussion

- The Antimicrobial Division of EPA asserts that additional toxicology studies are necessary on ECONEA to support the bridging of subchronic and chronic toxicology data from chlorfenapyr to its active metabolite CL303,268 (ECONEA). As such, the ECONEA file is deemed incomplete and the EPA files for the active substance (ECONEA Technical – 43813-ET) and end-use paint (NEXXIUM 20 – 11350-GL) have not been activated for review.

- Janssen et al. agree that while some additional toxicology information may be reasonable, the need for additional toxicology studies was not transparent at or following the pre-registration meeting of March 7, 2001. EPA's minutes of this pre-submission meeting have not been made available to the registrants following numerous requests. (Note: additional environmental fate and ecotoxicology studies that were deemed data gaps in March 2001 have been subsequently performed and were submitted with the original application file). Further, the bridging rationale was not requested by EPA for it's review at any time prior to the full file submission; the registrants and end-users are now being penalized, while following all EPA procedures and protocols for submission of a new active

1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000

us.janssen.com

ingredient. Janssen et.al. requests that the ECONEA and NEXXIUM files be put into review, acknowledging the toxicology considerations.

Janssen and BASF will meet separately with the AD scientific staff to clearly understand the toxicology bridging concerns and to plan and schedule additional appropriate studies.

- The Naval Sea Systems Command and the Environmental Protection Agency are currently working on a multi-year program to develop Uniform National Discharge Standards (UNDS) for a variety of constituents released from Navy ships including copper from antifouling paint. In addition to the UNDS effort, Navy facilities in Puget Sound, WA and San Diego, CA are under pressure from local water quality regulatory agencies to reduce copper emissions. In response to these issues, NAVSEA has a funded program to investigate copper-free antifouling coatings for potential use on Navy vessels. The ability of commercial paint suppliers to get copper-free coatings registered is of critical importance to NAVSEA because without registered, copper-free or reduced copper antifouling coatings, the NAVSEA program is unlikely to succeed.

- In view of the International Maritime Organization's ban on the application of antifouling paints beginning in 2003, the USEPA Antimicrobials Division (AD) has prioritized the review of alternative (non-tin containing) candidate antifouling products. ECONEA is non-persistent in the aquatic environment, with a hydrolytic breakdown ($t_{1/2}$=3 hours) in seawater at 25°C, into lower toxicity metabolites. Janssen has conducted a combined total of over 60 environmental fate and ecotoxicity studies on the parent compound and three main aquatic metabolites. Processing the ECONEA application at this time is consistent with both AD's priority setting and EPA's Water Division objectives through the UNDS program.

1125 TRENTON-HARBOURTON ROAD
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3/6/03 Eonea/EPA Toxicology Data Meeting

Attendance Sheet

Name	Organization	Phone#	FAX#	Email	Website
Dennis Edwards	EPA/AD	703-308-8087		edwards.dennis@epa.gov	
Tim Memahon	EPA/AD	703-308-6342		memahon.tim@epa.gov	
Jonathan Chen	EPA/AD	703-305-1287		jonathan.chen@epa.gov	
Charles Hastings	BASF	919-547-2551		hastinc@basf.com	
NADER ELKASSABANY	EPA/AD	703.308.8785		elkassabany.nader@epa.gov	
Kathryn Montague	EPA/AD	7033051243		montague.kathryn@epa.gov	
Karen Heeny	EPA/AD	703-308-6237		heeny.karen@epa.gov	
Norm Cook	EPA/AD	703-308-8253		cook.norm@epa.gov	
Marshall Swindell	EPA/AD	703-305-6341		Swindell.Marshall@EPA.gov	
Alberto Protzel	EPA/HED	703 305 5347		Protzel.Alberto@EPA.gov	
Bill Goodwine	JANSSEN	730-2607 (609)		BGOODWIN@JANUS.JNJ.com	
Piet Blancquaert	Janssen	+32 14 60 37 76		PBLANCQU@JANBE.JNJ.COM	
Frederick Hess	BASF	(919) 547-2004		hessf@basf-corp.com	

PRECAUTIONARY STATEMENT
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

DANGER

Fatal if swallowed. Corrosive. Causes irreversible eye damage. Do not get in eyes or on clothing. Wear protective eyewear such as goggles, face shield or safety glasses. Wash thoroughly with soap and water after handling and before eating, drinking, or using tobacco. Harmful if inhaled or absorbed through the skin. Avoid breathing dust. Avoid contact with skin, eyes, or clothing. Remove contaminated clothing and wash clothing before reuse.

FIRST AID	
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If inhaled	-Move person to fresh air. -If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. -Call a poison control center or doctor for further treatment advice
If on skin or clothing	-Take off contaminated clothing. -Rinse skin immediately with plenty of water for 15-20 minutes. -Call a poison control center or doctor for treatment advice.
HOT LINE NUMBER: Chem Trec: (800) 424-9300 Have the product container with you when calling a poison control center or doctor, or going for treatment	
NOTE TO PHYSICIAN Probable mucosal damage may contraindicate the use of gastric lavage.	

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Technical

Anti-fouling Preservative

For Formulating Use Only

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INERT INGREDIENTS:	6.8%
TOTAL:	100.0%

KEEP OUT OF REACH OF CHILDREN

DANGER **POISON**

See side panel for first aid and additional precautionary statements.

EPA Reg. No.:43813-XX
EPA Est. No.: 241-MO-001

NET Contents: 110 lbs. (50 kgs)

JANSSEN PHARMACEUTICA
1125 Trenton-Harbourton Road
Titusville, NJ 08560

04/02

DIRECTIONS FOR USE
It is a violation of Federal law to use this product in a manner inconsistent with its labeling.
This product is for formulation into anti-fouling products for control of hard fouling organisms. Each formulator is responsible for obtaining EPA registration for their end-use product(s).

STORAGE AND DISPOSAL
PROHIBITIONS: Do not contaminate water, food or feed by storage and disposal.
STORAGE: DO NOT mix or store this product or solutions of this product in a manner inconsistent with its labeling.
DISPOSAL: Pesticide wastes may be acutely hazardous. Improper disposal is a violation of Federal Law.
PESTICIDE DISPOSAL: Pesticide, mixtures, or equipment rinse waters that cannot be chemically reprocessed must be disposed of according to applicable federal, state or local procedures. Contact your State Pesticide or Environmental Control Agency or the Hazardous Waste representative at the nearest EPA Regional Office for guidance.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into formulation equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If burned, stay out of smoke. If drum is contaminated and cannot be reused, dispose of in the same manner.

ENVIRONMENTAL HAZARDS
Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

NOTICE OF WARRANTY
Janssen Pharmaceutica warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with the directions under normal use conditions. It is impossible to eliminate all risks inherently associated with the use of this product. Ineffectiveness or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of Janssen Pharmaceutica. In no case shall Janssen Pharmaceutica be liable for consequential, special or indirect damages resulting from the use or handling of this product. The Buyer shall assume all such risks. **Janssen Pharmaceutica makes no warranties of merchantability of fitness for a particular purpose or any other express or implied warranty except as stated above.**

ECONEA ANTIFOULANT

(EPA FILE SYMBOL 43813-ET)

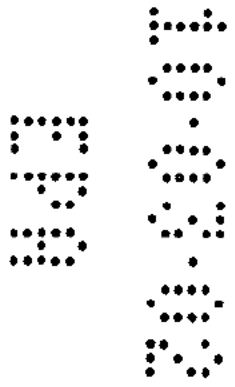
JANSSEN RESPONSE TO EPA COMMENTS

FOR NEW CHEMICAL SCREEN

DATE: September 26, 2002

SUBJECT:
- ➢Product Chemistry
- ➢Toxicology
- ➢Human Exposure

AUTHORS :		
	Fred Hess	BASF Corporation
	Mike Treacy	BASF Corporation
	Moorthy Mallipudi	BASF Corporation
	William Goodwine	Janssen Pharmaceutica Inc.



Pages 240-306 - *Access to FIFRA health and safety data is restricted under FIFRA

SUBMISSION BAR CODE # 6/85587 REVIEWER KL

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 43813-EJ PM 33 ACTION CODE 011

DESCRIPTOR Daphnia Studies on parent & 2 metabolites

[ ] CHILD RESISTANT PACKAGING:
[ ] CERTIFICATION
[ ] NON-RESIDENTIAL USE ONLY
[[NOT APPLICABLE

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL

PROPOSED CLASSIFICATION: [[GENERAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
6/24/02	7/1/02	7/8/02

METHOD OF SUPPORT

[ ] CITE-ALL
[ ] SELECTIVE
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

FORMULATORS EXEMPTION

[ ] SUBMITTED
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
EFFICACY				
TOXICOLOGY				
HED TOX.				
ENVIRON. FATE				
FISH/WILDLIFE	Studies added to current screen pass 7/15/02 (Nader			
OTHER				

STATUS

RESPONSE CODE RESPONSE DATE

JUN 24 2002

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

JANSSEN PHARM. RESEARCH FOUNDATION
P.O. BOX 200
1125 TRENTON-HARBOURTON ROAD
TITUSVILLE, NJ 085600200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 05/02/02. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

JANSSEN PHARMACEUTICA INC.

April 25, 2002

456958-00

Mr. Marshall Swindell
Product Manager Team 33
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

43813-ET

SUBJECT: ECONEA™ Technical (Janssen Code No. R107894)
Application for Registration
Antimicrobiat Division Priority Review to Replace TBTO by 2003

Dear Mr. Swindell:

Janssen Pharmaceutica Inc. is making an application for the registration of ECONEA™ Technical for formulation of antifouling treatment products under the general use pattern of aquatic non-crop. The USEPA Antimicrobial Division has indicated to the ACC Biocides Panel that TBTO replacement products for anti-fouling use would be given a priority for AD resources for expedited review.

Janssen is coordinating this submission with the submission by Sigma Coatings USA B.V. for end-use antifouling paints under the NEXXIUM™ brand of coatings. The regulatory contact for Sigma is Mr. Mike Winter [1-800-221-7978 (x247)].

The following administrative documents (1 copy) are provided:

Document	ECONEA Technical
Application for Pesticide Registration	X
Confidential Statement of Formula (CSF)	X
Certification with Respect to Citation of Data (Form 8570-34)	X
Data Support Matrices - Selective Method of Support (Form 8570-35)	X
Letters of Authorization for ECONEA & NEXXIUM from BASF Corporation	X
Specimen Label (6 copies)	X

1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000
us.janssen.com

A certification statement from Inveresk Research, dated April 17, 2002, is attached to this transmittal letter indicating that the pH of the test solution for the primary eye irritation study is < 2. Consistent with Agency guidelines, this study was not performed, and the technical active substance was categorized as corrosive to eyes for labeling.

Studies submitted by reference to the BASF Corporation file (see Letter of Authorization) for EPA Registration No. 241-366 include:

Study Type	MRID
Acute oral toxicity for AC 303,268 (R107894)	43492824
Acute oral toxicity for metabolite CL 322,250	43492826
Acute oral toxicity for metabolite CL 325,195	43492827
Freshwater fish LC50 (Bluegill) for metabolite CL 325,195	44452617
Acute LC50 freshwater invertebrate for metabolite CL 325,195	44452618
Avian oral LD50 for AC303268 (R107894) – Mallard Duck	43492808
Avian oral LD50 for metabolite CL 325,195 – Mallard Duck	44452612
Avian oral LD50 for AC303268 (R107894) – Bobwhite Quail	43492809
Avian oral LD50 for metabolite CL325,195 – Bobwhite Quail	44452611
All subchronic & chronic toxicology, mutagenicity and metabolism studies	See attached BASF data matrix for product registration 241-366

Data Evaluation Records (DERs) have been submitted for all studies submitted by reference to assist the Anti-Microbial Division in their review.

Supporting data included in the ECONEA application are comprised of three (3) copies each of the following reports:

PRODUCT CHEMISTRY (40 CFR 158.155, 160, 162, 167, 170, 175, 180, 190)

Volume 1 Preliminary Analysis and Certification of Ingredient Limits for the Technical Grade of AC 303268, Report No. APBR 1212, February 7, 2002, BASF, OPPTS Draft Guideline 830.1550, 830.1700 & 830.1750.

MRID 45695801

Volume 2 Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303268: OPPTS 830.1600, "Description of Materials Used to Produce Product" and OPPTS 830.1620, "Description of Product Process, Report No. P-363.01, January 22, 2001, BASF, OPPTS Draft Guideline 830.1600 & 830.1620.

MRID 45695802

Volume 3 Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303.268: OPPTS 830.1670, "Description of the Formation of Impurities", Report No. P-364.01, February 5, 2002, BASF, OPPTS Draft Guideline 830.1670.

MRID 45673901

Volume 4 Validation of the Ion Chromatographic Method M-3417.01 to Assay for Triethylamine (TEA) in the CL 303268 Technical Grade Active Ingredient (TGAI), Report No. APBR 1130, November 3, 2000, BASF, OPPTS Draft Guideline Reference 830.1700.

MRID 45673902

Volume 5 Validation of HRGC Method M-3467.01 to Assay for CL 312264 and CL 322697 in the Technical Grade of AC 303268, Report No. APBR 1153, February 27, 2001, BASF, OPPTS Draft Guideline Reference 830.1700

MRID 45673903

Volume 6 Validation of High Performance Liquid Chromatographic Method M-3397.03 to Assay for the Minor Components in CL 303268 Technical Grade Active Ingredient, Report No. APBR 1129, January 30, 2001, BASF, OPPTS Draft Guideline Reference 830.1700.

MRID 45673904

Volume 7 Validation of the High Performance Liquid Chromatographic Method M-3408 to Assay for CL 303268 in the Technical Grade Active Ingredient (TGAI), Report No. APBR 1109, March 25, 2002, BASF, OPPTS Draft Guideline Reference 830.1700 & 830.1800.

MRID 45673905

Volume 8 R107894: Determination of the Physico-Chemical Properties (pH, pKa, and EC Tests A4, A6 and A8), Report No. 1073/41-D2141 (Janssen Report No. AGR00301), January 2001, Covance Laboratories Ltd., OPPTS Draft Guideline Reference Series 63 (158.190).

MRID 45673906

Volume 9 R107894: Determination of Physico-Chemical Properties, Report No. 1073/48-D2149 (Janssen Report No. AGR00351), July 2001, Covance Laboratories Ltd. OPPTS Draft Guideline Reference Series 63 (158.190).

MRID 45673907

ENVIRONMENTAL FATE (40 CFR 158.290)

Volume 10 Determination of the Hydrolytic Stability of [14C]-R107894, Report No. 15348, December 22, 1997, Inveresk Research, Date Requirement 161-1.

MRID 45673908

Volume 11 Supplement to Hydrolytic Stability Report No. 15348-Identification of Hydrolytic Degradation Products of [14C]-R107894, Report No. 15365, December 17, 1997, Inveresk Research, Data Requirement 161-1.

MRID 45673909

Volume 12 The Anaerobic Degradation of [14C]-R107894 in Two Water/Sediment Systems, Report No. 17832, January 12, 2000, Inveresk Research, Data Requirement 162-3.

MRID 45673910

Volume 13 The Aerobic Degradation of [14C]-R107894 in Two Water/Sediment Systems, Report No. 16787, February 15, 1999, Inveresk Research, Data Requirement 162-4.

MRID 45673911

Volume 14 Supplement to Report No. 16787-The Aerobic Degradation of R107894 in Two Water/Sediment Systems, Report No. 17802, October 19, 1999, Inveresk Research, Data Requirement 162-4.

MRID 45673912

Volume 15 Adsorption/Desorption of [14C]-R107894 in Sediments, Report No. 15715, April 7, 1998, Inveresk Research, Data Requirement 163-1.

MRID 45673913

Volume 16 Adsorption/Desorption of the Hydrolysis Products of [14C]-R107894 in Sediments, Report No. 16693, January 22, 1999, Inveresk Research, Data Requirement 163-1.

MRID 45673914

Volume 17 Justification for waiver to conduct soil leaching studies with R107894 based on existing data and pesticide assessment guidance, Report No. 13751-6131, December 13, 2001, Springborn Laboratories, Inc., Guideline Reference 163-1.

MRID ADMIN

TOXICOLOGY (40 CFR 158.340)

ACUTE TOXICOLOGY

Volume 18 R107894 Technical Acute Oral Toxicity (Fixed Dose Procedure) Test in Rats, Report No. 19839, Janssen Report No. AGR308, November 20, 2001, Inveresk Research, OPPTS Draft Guideline 870.1100.

MRID 45673915

Volume 19 R107894 Technical Acute Dermal Toxicity (LD50) Test in Rats, Report No. 19836, Janssen Report No. AGR307, November 20, 2001, Inveresk Research, OPPTS Draft Guideline 870.1200.

MRID 45673916

Volume 20 R107894 Technical Acute Inhalation Toxicity Study in Rats, Report No. 19794 (Report Amendment), October 12, 2001, Inveresk Research, OPPTS Draft Guideline 870.1300.

MRID 45673917

Volume 21 R107894 Technical Acute Dermal Irritation Test in Rabbits, Report No. 20682, Janssen Report No. AGR306, January 11, 2002, Inveresk Research, OPPTS Draft Guideline 870.2500.

MRID 45673918

Volume 22 R107894 Technical Buehler Test in Guinea Pigs for Delayed Skin Sensitization Potential, Report No. 20973, Janssen Report No. AGR304, January 17, 2002, Inveresk Research, OPPTS Draft Guideline 870.2600.

MRID 45673919

Volume 23 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Acute Oral Toxicity for AC303,630 (R107894), and metabolites CL 322,250 & CL 325,195, Guideline 81-1

MRID 45673920

SUBCHRONIC TOXICITY

Volume 24 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 82-1 (870.3100), 82-1a (870.3150), 82-1b (870.3150), 82-2 (870-3200), 82-7 (870.6200), Subchronic Toxicity.

MRID ADMIN

CHRONIC TOXICITY

Volume 25 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 83-1b (870.4100), 83-3a (870.3700), 83-3b (870.3700), 83-4 (870.3800), 83-5 (870.4300), Chronic Toxicity.

MRID ADMIN

MUTAGENICITY

Volume 26 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 84-2 (870.5100), 84-2 (870.5300), 84-2 (870.5375), 84-2 (870.5395), 84-2 (870.5550), Mutagenicity.

MRID ADMIN

METABOLISM

Volume 27 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 85-1 (870.7485), Metabolism.

MRID ADMIN

ECO-TOXICITY (40 CFR 158.490)

Parent Compound R107894

Volume 28 Acute toxicity of R107894 technical fish, *Oncorhynchus mykiss*, Report No. WE-03-220, (Janssen Rpt. No. AGR 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID 45674001

Volume 29 Acute toxicity of R107894 technical for fish, *Lepomis macrochirus*, Report No. WE-03-227, (Janssen Rpt. No. AGR 294), April 15, 2002, LISEC, OPPTS Draft Guideline No. 850.1075

MRID 45674002

Volume 30 R107894-Acute Toxicity to Sheepshead Minnow (*Cyprinodon variegatus*) Under Flow-Through Conditions, Report No. 13751.6119 (Janssen Rpt. No. AGR 368), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1075.

MRID 45674003

Volume 31 Acute toxicity of R107894 technical for *Daphnia magna*, Report No. WE-01-250 (Janssen Rpt. No. AGR 298), December 10, 2001, LISEC, OPPTS Draft Guideline 850.1010

MRID 45674004

Volume 32 R107894-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6120 (Janssen Rpt. No. AGR 365), December 3, 2001, Springborn Labs, OPPTS Draft Guideline 850.1025.

MRID 45674005

Volume 33 R107894-Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions, Report No. 13751.6118 (Janssen Rpt. No. AGR 371), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1035.

MRID 45674006

Volume 34 R107894-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6128 (Janssen Rpt. No. AGR 383), November 6, 2001 Springborn Labs, OPPTS Draft Guideline 850.1400

MRID 45674007

Volume 35 *Daphnia magna* reproduction test of R107894 technical, Report No. WE-02-051, (Janssen Rpt. No. AGR 292), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674008

Volume 36 R107894-Life-Cycle Toxicity Test with Mysids *(Americamysis bahia)*, Report No. 13751.6107 (Janssen Rpt. No. AGR336), July 9, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1350

MRID 45674009

Volume 37 R107894-Toxicity to Amphipods *(Hyalella azteca)* During a 10-Day Sediment Exposure, Report No. 13751.6105 (Janssen Rpt. No. AGR 340), July 5, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45674010

Volume 38 R107894-Toxicity to Marine Amphipods *(Leptocheirus plumulosus)* During a 10-Day Sediment Exposure, Report No. 13751.6106 (Janssen Rpt. No. AGR 332), July 6, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674011

Volume 39 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Satisfying Avian LD50 Data Requirements for Mallard Ducks and Bobwhite Quail for AC303,630 (R107894 and Metabolite CL 325,195), Guideline 71-1

MRID 45695803

Metabolite CL 325,195

Volume 40 Acute toxicity of CL 325,195 for fish, *Oncorhynchus mykiss*, Report No. WE-03-219, (Janssen Rpt. No. AGR 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID 45674012

Volume 41 CL 325,195 - Acute Toxicity to Sheepshead Minnow (Cyprinodon variegatus) Under Flow-Through Conditions, Report No. 13751.6125 (Janssen Rpt. No. AGR 366), December 10, 2001, Springborn Laboratories. OPPTS Draft Guideline 850.1075.

MRID 45674013

Volume 42 CL325,195-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6126 (Janssen Rpt. No. AGR363), December 13, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1025.

MRID 45674014

Volume 43 CL325,195-Acute Toxicity to Mysids (Americamysis bahia) Under Flow-Through Conditions, Report No. 13751.6124 (Janssen Rpt. No. AGR 369), November 20, 2001, Springborn Laboratories, FIFRA Guideline Reference Number 72-3, OPPTS Draft Guideline 850.1035.

MRID 45674015

Volume 44 Fish, Early-life Stage Toxicity Test of CL 325,195 *(Danio rerio)*, Report No. WE-05-003 (Janssen Rpt. No. AGR 290), February 22, 2002, LISEC, OPPTS Draft Guideline 850.1400.

MRID 45674016

Volume 45 CL 325,195-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6130 (Janssen Rpt. No. AGR384), December 13, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1400

MRID 45674017

Volume 46 *Daphnia magna* reproduction test of CL 325,195, Report No. WE-02-050 (Janssen Rpt. No. AGR292), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674018

Volume 47 CL 325,195-Toxicity to Amphipods *(Hyalella azteca)* During a 10-Day Sediment Exposure, Report No. 13751.6116 (Janssen Rpt. No. AGR 343), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45674019

Volume 48 CL 325,195-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6117 (Janssen Rpt. No. AGR 335), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674020

Volume 49 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Satisfying Aquatic Acute LC50 Toxicity Data Requirements for Bluegill and *Daphnia magna* for Metabolite CL325,195, Guideline 72-1 & 72-2

MRID 45674021

Metabolite CL 322,250

Volume 50 Acute toxicity of CL 322,250 for fish, *Oncorhynchus mykiss*, Report No. WE-03-221 (Janssen Rpt. No. 296), January 9, 2002, LISEC, OPPTS Draft Guidaline 850.1075.

MRID 45674022

Volume 51 Acute toxicity of CL 322,250 for fish, *Lepomis macrochirus*, Report No. WE-03-228 (Janssen Rpt. No. AGR294), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1075

MRID 45674023

Volume 52 CL 322,250 - Acute Toxicity to Sheepshead Minnow (Cyprinodon variegatus) Under Flow-Through Conditions, Report No. 13751.6122 (Janssen Rpt. No. AGR 367), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1075.

MRID 45674101

Volume 53 Acute toxicity of CL 322,250 for *Daphnia magna*, Report No. WE-01-251 (Janssen Rpt. No. AGR 298), December 7, 2001, LISEC, OPPTS Draft Guideline 850.1010

MRID 45674102

Volume 54 CL322,250-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6123 (Janssen Rpt. No. AGR 364), December 10, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1025.

MRID 45674103

Volume 55 CL 322,250 - Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions, Report No. 13751.6121 (Janssen Rpt. No. AGR 370), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1035.

MRID 45674104

Volume 56 Fish, Early-life Stage Toxicity Test of CL 322,250 *(Danio rerio)*, Report No. WE-05-005 (Janssen Report No. AGR 290), February 22, 2002, LISEC, OPPTS Draft Guideline 850.1400.

MRID 45674105

Volume 57 CL 322,250-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6129 (Janssen Rpt. No. AGR 385), November 6, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1400

MRID 45674106

Volume 58 *Daphnia magna* reproduction test of CL 322,250, Report No. WE-02-052, (Janssen Rpt. No. AGR 292), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674107

Volume 59 CL 322,250-Toxicity to Amphipods (*Hyalella azateca*) During a 10-Day Sediment Exposure, Report No. 13751.6109 (Janssen Rpt. No. AGR 341), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45674108

Volume 60 CL 322,250 - Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6110 (Janssen Rpt. No. AGR 333), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674109

Metabolite CL 322,248

Volume 61 Acute toxicity of CL 322,248 for fish, *Oncorhynchus mykiss*, Report No. WE-03-223, (Janssen Rpt. No. AGR296), December 10, 2001, LISEC, OPPTS Draft Guideline 850.1075

MRID 45674110

Volume 62 Acute toxicity of CL 322,248 for fish, *Lepomis machrochirus*, Report No. WE-03-229, (Janssen Rpt. No. AGR294), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1075

MRID 45674111

Volume 63 Acute toxicity of CL 322,248 for *Daphnia magna*, Report No. WE-01-263, (Janssen Rpt. No. AGR 298), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1010

MRID 45674112

Volume 64 *Daphnia magna* reproduction test of CL 322,248, Report No. WE-02-054 (Janssen Rpt. No. AGR 292), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID 45674113

Volume 65 CL 322,248 - Toxicity to Amphipods (*Hyalella azateca*) During a 10-Day Sediment Exposure, Report No. 13751.6112 (Janssen Rpt. No. AGR 342), October 11, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID 45695804

Volume 66 CL 322,248-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6113 (Janssen Rpt. No. AGR 334), October 11, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID 45674114

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Parent Compound R107894

Volume 67 R107894-Determination of Effects on Seedling Emergence of Rice (*Oryza sativa*), Report No. 13751.6127 (Janssen Rpt. No. AGR362), October 23, 2001, Springborn Labs, OPPTS Draft Guidelines 850.4100 and 850.4225.

MRID 45674115

Volume 68 R107894-Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6104, (Janssen Rpt. No. AGR 337), April 24, 2001,Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674116

Volume 69 Alga, growth inhibition test effect of R107894 technical on the growth of *Raphidocelis subcapitata*, Report No. WE-06-261 (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674117

Volume 70 Alga, growth inhibition test effect of R107894 technical on the growth of *Skeletonema costatum*, Report No. WE-06-270 (Janssen Rpt. No. AGR 307), April 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID 45674118

Metabolite CL 325,195

Volume 71 CL 325,195 - Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6115 (Janssen Rpt. No. AGR 344), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674119

Volume 72 Alga, growth inhibition test effect of CL 325,195 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-260, (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674120

Volume 73 Alga, growth inhibition test effect of CL 325,195 on the growth of *Skeletonema costatum*, Report No. WE-06-269,(Janssen Rpt. No. AGR 309), February 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID 45674121

Metabolite CL 322,250

Volume 74 CL 322,250-Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6108 (Janssen Rpt. No. AGR 338), October 12, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674122

Volume 75 Alga, growth inhibition test effect of CL 322,250 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-262 (Janssen Report No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID 45674123

Volume 76 Alga, growth inhibition test effect of CL 322,250 on the growth of *Skeletonema costatum*, Report No. WE-06-271, (Janssen Rpt. No. 309), February 15, 2002, LISEC, OPPTS Data Guideline 850.5400

MRID 45674124

Metabolite CL 322,248

Volume 77 CL 322,248 - Toxicity to Duckweed, *Lemna gibba* Report No. 13751.6111 (Janssen Rpt. No. AGR 339), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID 45674125

Volume 78 Alga, growth inhibition test effect of CL 322,248 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-266 (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Data Guideline 850.5400.

MRID 45674126

Volume 79 Alga, growth inhibition test effect of CL 322,248 on the growth of *Skeletonema costatum*, Report No. WE-06-272, (Janssen Rpt. No. AGR 309), February 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID 45674127

OCCUPATIONAL EXPOSURE

Volume 80 Screening level occupational exposure assessments for R107894 (CL303268) as an anti-foulant in paint applied to underwater hulls, EXP Project No. 47101, EXP Report No. 02001, January 11, 2002, EXP Corporation, OPPTS Draft Guideline Series 875.

MRID 45674128

Please consider assigning priority review status to this action since it satisfies the criteria as a TBTO replacement for anti-fouling use; TBTO will no longer be allowed by the International Maritime Organization (IMO) after 2003. The USEPA Antimicrobial Division has identified TBTO anti-fouling replacement products as a priority for receiving a high level of EPA resources in 2002-03 work plan.

Please contact me directly on any matters relating to this registration application. I can be reached by phone at 609-730-2607.

Sincerely,

Bill Goodwine

William R. Goodwine
Director
Plant & Material Protection Division

Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.inj.com

JUL 08 2002

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

JANSSEN PHARM. RESEARCH FOUNDATION
P.O. BOX 200
1125 TRENTON-HARBOURTON ROAD
TITUSVILLE, NJ 085600200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 07/01/02. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

JANSSEN PHARMACEUTICA INC.

June 24, 2002

Mr. Marshall Swindell
Product Manager Team 33
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

SUBJECT: ECONEA™ Technical (Janssen Code No. R107894)
Supplementary Data Submission
EPA File Symbol: 43813-ET
Antimicrobial Division Priority Review to Replace TBTO by 2003

Dear Mr. Swindell:

Janssen Pharmaceutica Inc. is making a supplementary data submission for the registration of ECONEA™ Technical for formulation of antifouling treatment products under the general use pattern of aquatic non-crop. Our primary submission was sent to the US EPA on April 25, 2002 with receipt acknowledged on May 2, 2002 (OPP Identification Number 294604). The USEPA Antimicrobial Division has indicated to the ACC Biocides Panel that TBTO replacement products for anti-fouling use would be given a priority for AD resources for expedited review.

The end use antifouling paint product (Nexxium 20), containing ECONEA was submitted by Sigma Coatings on April 20, 2002 and assigned EPA file symbol 11350-GL.

Three (3) copies each of the following reports along with Data Support Matrices are enclosed.

ECO-TOXICITY (40 CFR 158.490)
Parent Compound R107894

Volume 1 Acute toxicity of R107894 for *Daphnia magna*, Report No. WE-01-279, (Janssen Rpt. No. AGR 448), June 14, 2002, LISEC, OPPTS Draft Guideline 850.1010.

45706901

MRID

1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000
us.janssen.com

Metabolite CL 325,195

Volume 2 Acute toxicity of CL 325,195 for *Daphnia magna*, Report No. WE-01-281, (Janssen Rpt. No. AGR 450), June 14, 2002, LISEC, OPPTS Draft Guideline 850.1010.

MRID 45706902

Metabolite CL 322,250

Volume 3 Acute toxicity of CL 322,250 for *Daphnia magna*, Report No. WE-01-280 (Janssen Rpt. No. 449), June 14, 2002, LISEC, OPPTS Draft Guideline 850.1010.

MRID 45706903

As mentioned in my letter of April 25, 2002, please consider assigning priority review status to this action since it satisfies the criteria as a TBTO replacement for anti-fouling use; TBTO will no longer be allowed by the International Maritime Organization (IMO) after 2003. The USEPA Antimicrobial Division has identified TBTO anti-fouling replacement products as a priority for receiving a high level of EPA resources in 2002-03 work plan.

Please contact me directly on any matters relating to this registration application. I can be reached by phone at 609-730-2607.

Sincerely,

Bill Goodwine

William R. Goodwine
Director
Plant & Material Protection Division
Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com

Administrative Materials

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to this address.

DATA MATRIX

Date June 24, 2002	EPA Reg No./File Symbol 43813	Page 1 of 3
Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Eco-Toxicity - Parent Compound R107894

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.1010	Aquatic invertebrate acute tox, test, freshwater daphnids		Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	June 24, 2002

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version.

Agency Internal Use Copy

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DATA MATRIX

Date June 24, 2002	EPA Reg No./File Symbol 438 f3	Page 1 of 3
Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Eco-Toxicity - Parent Compound R107894

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	June 24, 2002

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Date June 24, 2002	EPA Reg No./File Symbol 438t3	Page 2 of 3
Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Eco-Toxicity - Metabolite CL 325,195

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.1010	Aquatic invertebrate acute tox, test, freshwater daphnids		Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Eco-Toxicity - Metabolite Cl, 325,195

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	June 24, 2002

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Eco-Toxicity - Matabolite CL 322,250

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.1010	Aquatic invertebrate acute tox, test, freshwater daphnids		Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	June 24, 2002

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Ingredient R107894 Eco-Toxicity - Metabolite CL 322,250

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	June 24, 2002

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version.

Public File Copy

Janssen
Antifoulant-

Kathryn Montague
04/26/01 04:15 PM

To: Winston Dang/DC/USEPA/US@EPA
cc: Norm Cook/DC/USEPA/US@EPA
Subject: Janssen antifoulant data requirements--eco (meeting minutes)

Winston,

Here is a more useable summary of the eco data requirements:

"AD/RASSB has determined that the following studies are OUTSTANDING and must be submitted to support the registration of this antifoulant (parent compound):

72-3a Estuarine/marine organism acute toxicity testing--fish
72-3b Estuarine/marine organism acute toxicity testing--oyster
72-3c Estuarine/marine organism acute toxicity testing--mysid
123-1 Terrestrial Plant Tier II Seedling Emergence test--rice (*Oryza sativa*) only
123-2 Aquatic Plant Tier II Testing--2 outstanding species (1 diatom and 1 blue-green algal

The company has also agreed to submit a rationale for ecological effects toxicity testing with one or more of the degradates of this chemcal . Additional data may be required pending review of this rationale.

Additionally, any data listed in the chart (provided with original meeting material) that the company has already generated or agreed to generate should be submitted."

Hope this helps!
Kay

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN - 2 2003

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

December 20, 2002

MEMORANDUM

SUBJECT: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(triflouromethyl)-; CL 303268: Response to the registrant's rebuttal to toxicology issues raised from the New Chemical Screen of CL 303268.

EPA Identification Numbers:

P.C. Codes: 119093

MRID's: N/A (correspondence)
DP Barcode: D286238

TO: Marshall Swindell/Karen Leavy-Munk
Regulatory Management Branch II / PM Team 33
Antimicrobials Division (7510C)

FROM: Timothy F. McMahon, Ph.D. 12/20/02
Senior Toxicologist
Antimicrobials Division (7510C)

THRU: Nader Elkassabany, Ph.D. NE 12/20/02
Team Leader, Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

and

Norm Cook, Chief 01.02.03
RASSB
Antimicrobials Division (7510C)

Action Requested: Respond to the registrant's rebuttal regarding bridging of toxicology data for chlorfenapyr to the chlorfenapyr metabolite CL 303268 to support the registration of CL 303268 as an active ingredient in the antifouling paint product Sigma Nexxium 20 Antifouling, and the technical material (Econea antifouling preservative)..

Background

Janssen Phamaceutical, Titusville, New Jersey, previously submitted applications to the Environmental Protection Agency for registration of the manufacturing-use product ECONEA technical (containing 93.2% CL 303268 as active) and the formulated product Sigma Nexxium 20 Antifouling (containing CL 303268 at 3.4% and C9-211 at 3.4%)

The registrant put forth the proposal that toxicology data for the parent compound chlorfenapyr could be bridged to address toxicity of the CL 393268 metabolite. The registrant used several lines of argument. As stated in the previous memo and repeated here for continuity, the primary argument is that the mode of action of chlorfenapyr can be attributed to the CL 303268 metabolite (from page 11 of the submitted discussion: " the insecticidal activity of parent chlorfenapyr can be attributed to CL 303268. CL 303268 was shown to be an extremely potent insecticide with LC50 values of < 10 ppm against southern armyworms and tobacco budworms. In addition, the mammalian toxicity of chlorfenapyr can be attributed to CL 303268, as CL 303268 was shown to be highly toxic to mammals by the acute oral route.") [Note: This claim is based on the following: the LC50 value of the CL 303268 metabolite is very low, i.e. < 10ppm. also, the acute oral toxicity of this metabolite is lower (27-29 mg/kg/day) vs. the parent (441(M) and 1152 (F) mg/kg/day)].

In response to the registrant's submission, the Antimicrobials Division pointed out (in memorandum D284098) that the mode of action for chlorfenapyr had never been previously submitted to the Agency for review, and that arguments supporting the CL 303268 metabolite as the proximate species responsible for the insecticidal activity of chlorfenapyr would have to be examined by the Agency.

Discussion

Chlorfenapyr is registered with the Office of Pesticide Programs as an agricultural use pesticide. Specifically, chlorfenapyr is an insecticide-miticide for use on cotton, vegetables, citrus and ornamentals A temporary tolerance has been established in/on cottonseed at 0.5 ppm (PP#5F04456). Temporary tolerances of 0.5 ppm have also been proposed for oranges and lemons (PP#5G04507).

The registrant submitted additional data in support of the conclusion that the CL 303268 metabolite is an uncoupler of oxidative phosphorylation (Black, B.C. et al., *Insecticidal Action*

and Mitochondrial Uncoupling Activity of AC-303,630 and Related Halogenated Pyrroles, Pesticide Biochemistry and Physiology Vol. 50: pp. 115-128, 1994; Hunt, D.A. and Treacy, M.F.: Pyrrole Insecticides: A New Class of Agriculturally Important Insecticides Functioning as Uncouplers of Oxidative Phosphorylation; In Ishaaya I. and D. Degheele (eds.), Insecticides with novel modes of action: mechanism and application, Springer-Verlag, New York, Berlin, Chapter 8, pages 139-151, 1997; Gange, D.M., et al., The QSAR of Insecticidal uncouplers. In Hansch, C. and T. Fujita (eds.). Classical and three-dimension QSAR in agrochemistry, American Chemical Society, Chapter 15: pages 199-212, 1995). These data do appear to support the argument that CL 303268 does possess this property.

Examination of the toxicity database for chlorfenapyr shows that the liver is a target organ of toxicity for chlorfenapyr. In the 28-day dermal toxicity study in the rabbit and in carcinogenicity studies in the rat, the primary toxic effects observed were in the liver (increased cholesterol, increased liver weight and cytoplasmic vacuolation in the 28-day study; hepatocellular adenoma in male rats in the carcinogenicity study in rats). In addition, a one-year neurotoxicity study in rats and a chronic toxicity/carcinogenicity study in mice showed significant nervous system toxicity, including vacuolation of the central nervous system (brain, spinal cord, optic nerve). The toxicity of chorfenapyr to the liver is not likely related to the proposed mechanism of action, i.e. uncoupling of oxidative phosphoryation, but some other mechanism. The central nervous system toxicity on the other hand could be possibly related to the uncoupling effect. As noted in Chapter 16 of Casarett and Doulls' Fifth Edition of Toxicology: The Basic Science of Poisons (1996), " Neurons are highly dependent upon aerobic metabolism for energy requirements. Cells of the nervous system must be able to produce large quantities of high energy phosphates even at rest to meet the demand for maintenance and repetitive reinstitution of ion gradients necessary for membrane depolarization and repolarization." "The systemic exposure to toxicants that inhibit aerobic respiration, such as cyanide...leads to the earliest signs of dysfunction in the myocardium and neurons." Thus, even a brief interruption in the energy supply to neurons will be detrimental, as the nervous system is more sensitive to the effects of oxidative phosphorylation uncoupling than other systems in the body.

There is not enough submitted toxicity data for the CL 303268 metabolite to establish whether there is any concordance in toxicity between parent chlorfenapyr and the CL 303268 metabolite. The proposed mode of action for the CL 303268 metabolite is not entirely reflective of the toxicity of chlorfenapyr. There are likely differences in the dose-response for toxicity between the parent chlofenapyr and the CL 303268 metabolite, which is partially evident when comparing the acute oral LD50 values between the two compounds as noted above.

Conclusions

The lack of concordance in the toxicity between chlofenapyr and the CL 303268 metabolite and the lack of data for the two compounds demonstrating any concordance does not support using the toxicity database for chlofenapyr to support registration of the CL 303268 metabolite. In addition, the signs of neurotoxicity produced in long-term studies with chlorfenapyr needs to be investigated further with respect to the CL 303268 metabolite, as this metabolite, through the uncoupling mechanism, may have some relationship to the neurotoxic effects observed with chlorfenapyr . If the CL 303268 metabolite is in fact the proximal toxicant, its neurotoxicity might even be higher than that of the parent. It is very possible that the toxicity of the CL 303268 metabolite is different than the toxicity of parent chlorfenapyr from the available data. Neurotoxic effects are of particular concern.

In order to better establish the relationship of the CL 303268 metabolite to chlorfenapyr, the registrant will need to conduct the following studies with the CL 303268 metabolite: a 90-day oral toxicity study with neurotoxicity endpoints included in the study design, a developmental toxicity study in the rat, and a mutagenicity testing battery (the registrant appears to already have an Ames assay, but needs to complete the testing battery with two other studies). In this way, the toxicity of the parent chlorfenapyr realtive to CL 303268 metaoblite can be assessed and a decision can be made as to whether these studies are adequate to bridge toxicity data from the parent for this metabolite.

)P BARCODE: D286238

CASE: 072289 DATA PACKAGE RECORD DATE: 01/03/03
)UBMISSION: S623573 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

)ASE TYPE: REGISTRATION ACTION: 011 RESUB NEW CHEM SCRNG
)HEMICALS: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)- 99.0000%

ID#: 043813-ET ECONEA TECHNICAL
)OMPANY: 043813 JANSSEN PHARMACEUTICA
)RODUCT MANAGER: 33 MARSHALL SWINDELL 703-308-6341 ROOM: CS1 6B
)M TEAM REVIEWER: KAREN LEAVY-MUNK 703-308-6237 ROOM: CS1 6W9
RE[redacted]VED DATE: 10/03/02 DUE OUT DATE: 01/01/03

* * * DATA PACKAGE INFORMATION * * *

)P BARCODE: 286238 EXPEDITE: Y DATE SENT: 10/18/02 DATE RET.: 01/02/03
)HEMICAL: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)-5-(triflu
)P TYPE: 001
CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT	ADMIN DUE DATE: 11/17/02
DIV : AD	10/18/02	01/02/03	NEGOT DATE: / /
BRAN: RASSB	10/18/02	01/02/03	PROJ DATE: / /
SECT: RASSB2	10/18/02	12/20/02	
REVR : TMCMAHON	10/23/02	12/20/02	
CONTR:	/ /	/ /	

* * * DATA REVIEW INSTRUCTIONS * * *

Norm this was sent through RASSB for tracking purposes and so that you would be aware of what's going on.
Please forward this rebuttal to AD's screening of the ECONEA antifoulant new chem tox comments. Please forward to Tim for review. Tim indicated that he will work on it and confer with HED. When done we will schedule a meeting with the company. Thanks, Karen Leavy/Swindell
If any additional information is needed please contact Karen (308-6237).

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN - 2 2003

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

December 20, 2002

SUBJECT: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)-; CL 303268: Response to the registrant's rebuttal to toxicology issues raised from the New Chemical Screen of CL 303268.

EPA Identification Numbers:

P.C. Codes: 119093

MRID's: N/A (correspondence)
DP Barcode: D286238

TO: Marshall Swindell/Karen Leavy-Munk
Regulatory Management Branch II / PM Team 33
Antimicrobials Division (7510C)

FROM: Timothy F. McMahon, Ph.D. 12/20/02
Senior Toxicologist
Antimicrobials Division (7510C)

THRU: Nader Elkassabany, Ph.D. NE 12/20/02
Team Leader, Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

and

Norm Cook, Chief 01-02-03
RASSB
Antimicrobials Division (7510C)

Action Requested: Respond to the registrant's rebuttal regarding bridging of toxicology data for chlorfenapyr to the chlorfenapyr metabolite CL 303268 to support the registration of CL 303268 as an active ingredient in the antifouling paint product Sigma Nexxium 20 Antifouling, and the technical material (Econea antifouling preservative). .

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The registrant put forth the proposal that toxicology data for the parent compound chlorfenapyr could be bridged to address toxicity of the CL 393268 metabolite. The registrant used several lines of argument. As stated in the previous memo and repeated here for continuity, the primary argument is that the mode of action of chlorfenapyr can be attributed to the CL 303268 metabolite (from page 11 of the submitted discussion: " the insecticidal activity of parent chlorfenapyr can be attributed to CL 303268. CL 303268 was shown to be an extremely potent insecticide with LC50 values of < 10 ppm against southern armyworms and tobacco budworms. In addition, the mammalian toxicity of chlorfenapyr can be attributed to CL 303268, as CL 303268 was shown to be highly toxic to mammals by the acute oral route.") [Note: This claim is based on the following: the LC50 value of the CL 303268 metabolite is very low, i.e. < 10ppm. also, the acute oral toxicity of this metabolite is lower (27-29 mg/kg/day) vs. the parent (441(M) and 1152 (F) mg/kg/day)].

In response to the registrant's submission, the Antimicrobials Division pointed out (in memorandum D284098) that the mode of action for chlorfenapyr had never been previously submitted to the Agency for review, and that arguments supporting the CL 303268 metabolite as the proximate species responsible for the insecticidal activity of chlorfenapyr would have to be examined by the Agency.

Discussion

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Conclusions

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)P BARCODE: D286238

CASE: 072289 DATA PACKAGE RECORD DATE: 01/03/03
)UBMISSION: S623573 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

)ASE TYPE: REGISTRATION ACTION: 011 RESUB NEW CHEM SCRNG
)HEMICALS: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)- 99.0000%

ID#: 043813-ET ECONEA TECHNICAL
)OMPANY: 043813 JANSSEN PHARMACEUTICA
)RODUCT MANAGER: 33 MARSHALL SWINDELL 703-308-6341 ROOM: CS1 6B
)M TEAM REVIEWER: KAREN LEAVY-MUNK 703-308-6237 ROOM: CS1 6W9
RE[redacted]VED DATE: 10/03/02 DUE OUT DATE: 01/01/03

* * * DATA PACKAGE INFORMATION * * *

)P BARCODE: 286238 EXPEDITE: Y DATE SENT: 10/18/02 DATE RET.: 01/02/03
)HEMICAL: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)-5-(triflu
)P TYPE: 001
CSF: N LABEL: N

ASS[redacted]GNED TO	DATE IN	DATE OUT	ADMIN DUE DATE: 11/17/02
DIV : AD	10/18/02	01/02/03	NEGOT DATE: / /
BRAN: RASSB	10/18/02	01/02/03	PROJ DATE: / /
SECT: RASSB2	10/18/02	12/20/02	
REVR : TMCMAHON	10/23/02	12/20/02	
CONTR:	/ /	/ /	

* * * DATA REVIEW INSTRUCTIONS * * *

Norm this was sent through RASSB for tracking purposes and so that you would be aware of what's going on.
Please forward this rebuttal to AD's screening of the ECONEA antifoulant new chem tox comments. Please forward to Tim for review. Tim indicated that he will work on it and confer with HED. When done we will schedule a meeting with the company. Thanks, Karen Leavy/Swindell
If any additional information is needed please contact Karen (308-6237).

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN - 2 2003

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

December 20, 2002

MEMORANDUM

SUBJECT: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(triflouromethyl)-; CL 303268: Response to the registrant's rebuttal to toxicology issues raised from the New Chemical Screen of CL 303268.

EPA Identification Numbers:

P.C. Codes: 119093

MRID's: N/A (correspondence)
DP Barcode: D286238

TO: Marshall Swindell/Karen Leavy-Munk
Regulatory Management Branch II / PM Team 33
Antimicrobials Division (7510C)

FROM: Timothy F. McMahon, Ph.D. 12/24/02
Senior Toxicologist
Antimicrobials Division (7510C)

THRU: Nader Elkassabany, Ph.D. NE 12/20/02
Team Leader, Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

and

Norm Cook, Chief 01-02-03
RASSB
Antimicrobials Division (7510C)

Action Requested: Respond to the registrant's rebuttal regarding bridging of toxicology data for chlorfenapyr to the chlorfenapyr metabolite CL 303268 to support the registration of CL 303268 as an active ingredient in the antifouling paint product Sigma Nexxium 20 Antifouling, and the technical material (Econea antifouling preservative). .

Background

Janssen Phamaceutical, Titusville, New Jersey, previously submitted applications to the Environmental Protection Agency for registration of the manufacturing-use product ECONEA technical (containing 93.2% CL 303268 as active) and the formulated product Sigma Nexxium 20 Antifouling (containing CL 303268 at 3.4% and C9-211 at 3.4%)

The registrant put forth the proposal that toxicology data for the parent compound chlorfenapyr could be bridged to address toxicity of the CL 393268 metabolite. The registrant used several lines of argument. As stated in the previous memo and repeated here for continuity, the primary argument is that the mode of action of chlorfenapyr can be attributed to the CL 303268 metabolite (from page 11 of the submitted discussion: " the insecticidal activity of parent chlorfenapyr can be attributed to CL 303268. CL 303268 was shown to be an extremely potent insecticide with LC50 values of < 10 ppm against southern armyworms and tobacco budworms. In addition, the mammalian toxicity of chlorfenapyr can be attributed to CL 303268, as CL 303268 was shown to be highly toxic to mammals by the acute oral route.") [Note: This claim is based on the following: the LC50 value of the CL 303268 metabolite is very low, i.e. < 10ppm. also, the acute oral toxicity of this metabolite is lower (27-29 mg/kg/day) vs. the parent (441(M) and 1152 (F) mg/kg/day)].

In response to the registrant's submission, the Antimicrobials Division pointed out (in memorandum D284098) that the mode of action for chlorfenapyr had never been previously submitted to the Agency for review, and that arguments supporting the CL 303268 metabolite as the proximate species responsible for the insecticidal activity of chlorfenapyr would have to be examined by the Agency.

Discussion

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DP BARCODE: D286238

CASE: 072289 DATA PACKAGE RECORD DATE: 01/03/03
SUBMISSION: S623573 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REGISTRATION ACTION: 011 RESUB NEW CHEM SCRNG
CHEMICALS: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)- 99.0000%

ID#: 043813-ET ECONEA TECHNICAL
COMPANY: 043813 JANSSEN PHARMACEUTICA
PRODUCT MANAGER: 33 MARSHALL SWINDELL 703-308-6341 ROOM: CS1 6B
PM TEAM REVIEWER: KAREN LEAVY-MUNK 703-308-6237 ROOM: CS1 6W9
RECEIVED DATE: 10/03/02 DUE OUT DATE: 01/01/03

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 286238 EXPEDITE: Y DATE SENT: 10/18/02 DATE RET.: 01/02/03
CHEMICAL: 119093 Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorohoenyl)-5-(triflu
DP TYPE: 001
CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT	ADMIN DUE DATE: 11/17/02
DIV : AD	10/18/02	01/02/03	NEGOT DATE: / /
BRAN: RASSB	10/18/02	01/02/03	PROJ DATE: / /
SECT: RASSB2	10/18/02	12/20/02	
REVR : TMCMAHON	10/23/02	12/20/02	
CONTR:	/ /	/ /	

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No evaluation is written for this data package

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL

Reference Number 5617867

Input Date _____

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

File Symbol/Reg. No. 43813-ET PM 33 [18] Action Code 011

[10] Descriptor (Amend/Resubmissions only) _____

[5] Intrastate Call-In ☐ (Y) Yes ☐ (N) No

☐ Child-Resistant Packaging

☐ (C) Certification

☐ (S) Service Person

[20] Registration Type:

☐ (1) Conditional ☐ (2) Unconditional

☐ (R) Non-Residential Use Only

☐ (N) Not-Applicable

[25] Proposed Classification: [30] Final Classification

☐ (R) Restricted ☐ (R) Restricted

☐ (G) General ☐ (N) Not Classified

[35] Date on Application: 04 / 15 / 02 (MO / DAY / YR)

[04] EPA Received Dated: 06 / 17 / 02 (MO / DAY / YR)

[40] Date Received by PM: 06 / 24 / 02 (MO / DAY / YR)

[80] Method of Support:

☐ (1) Cite-All ☐ (6) Owner Submission

☐ (2) Not Applicable ☐ (7) Total Submission

☐ (3) Not Submitted ☐ (8) Selective Method

Reviewers Requested:	DATE SENT	DUE DATE	DATE RETURNED	RESPONSE CODE	RESPONSE DATE
RD					
PM					
PL					
CH					
EF					

[108] Status: Refer to the letter dated 8/14/02 with the corresponding submission dated 4/12/02

[115] FINAL ACTION Response Code 7

[120] Response Date 08 / 14 / 02

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 1 4 2002

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. William Goodwine
Janessen Pharmaceutica, Inc.
11215 Trenton-Harbourton Road
Titusville, JN 08560

Subject: ECONEA Technical
EPA File Symbol 43818-ET
Your Application Dated April 12th, 2002
EPA Received Date May 2nd, 2002

The application referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, is unacceptable for the following reasons:

Upon the conducting a new chemical screen on, ECONEA, the following deficiencies have been determined.

CHEMISTRY

The following studies were missing from the initial submission of data to support the chemical screen.

a) 830.6317 Storage and Stability Study- It was stated that the technical is stable for five years. The Agency is requesting a study to support this claim.

b) 830.6320 Corrosion Characteristics Study- The product information sheet states that the chemical is non-corrosive. The Agency is requesting a study to support this claim.

TOXICITY

The bridging data are insufficient to support the claims that the insecticide action of chlorfenapyr

is due to uncoupling of oxidative phosphorylation by the CL 303268 metabolite of chlorfenappyr. Therefore, the toxicology data for chlorfenapyr cannot be used to support hazard identification for the metabolite.

These are the issues that need to be addressed by the company before EPA can initiate any type of formal review of this data by the agency.

1) There are no data by the company to show that the CL 303268 metabolite is actually insecticidal by the proposed mode of action.

2) There are no submitted data the this metabolite ALONE is responsible for this mode of action (there are at least 5 metabolites of chlorfenapyr in mammalian studies sub-

3) There is no proof that any of the other metabolites of chlorfenapyr may or may not also work by this mode of action.

4) The disposition of the CL 303268 metabolite ay be quite different when administered directly compared to disposition of this metabolite when parent chemical is administered. The spectrum of toxicity of the metabolite may thus also be different.

5) Conduct of an acute oral toxicity study and a preliminary 28 day toxicity study with the CL 303268 metabolite is insufficient to make any claims supporting the mode of action.

Normally, to support toxicity claims between a parent chemical and a metabolite of that chemical, bridging data are submitted as one aspect of the data needed. The Office of Pesticide Programs requests a 90-day oral toxicity study, a developmental toxicity study, and at least one mutagenicity study as bridging data. These studies must be conducted according to the OPPTS harmonized test guidelines, Series 870. These data are necessary to determine if the spectrum of toxicity is the same between the parent chemical and the metabolite and to ger a reasonable idea of the relative potency of the toxicity of the compounds.

ECOLOGICAL EFFECTS

The submitted studies appear to be adequate for review and have passed the new chemical screen. However, pore water studies and avian reproductive studies may be requested once the data from the required studies are reviewed. These studies are reserved based on the findings from Tier II environmental studies.

ENVIRONMENTAL FATE

The submitted studies appear to be adequate for review and have passed the new chemical screen.

EXPOSURE

Human Exposure data requirements for MPs are not impeded by the Agency. However, the draft product labeling provided for ECONEA Technical is incomplete. Provide detailed information on the industrial mixing, loading and application processes, and any post-application worker (by stander) tasks anticipated when using this MP to formulate antifoulant paint end-use products.

Refer to the following human exposure data guidelines to develop this needed information:

GLN 875.1700 & 875.2700 Product Use Information

GLN 875.2800 Description of Human Activity

The findings of the actual review will not be complete without a full battery of toxicity data.

A complete copy of all the science memos are enclosed for your records.

The product mentioned above has failed the new chemical screen. The data will not be put into review until the above discrepancies have been clarified.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,

Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)

Reviewer ID KL

Submission No. 617866

Data Package No. _____

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

File Symbol/Reg. No. 43813-ET PM 33 Action Code 010

|10| Descriptor (Amend/Resubmisions only) _____

|5| Intrastate Call-in ☐ (Y) Yes ☐ (N) No

|15| Child-resistant Packaging ☐ (C) Certification ☐ (S) Service Person ☐ (R) Non-residential Use Only ☐ (N) Not-Applicable

|20| Registration Type:

☐ (1) Conditional ☐ (2) Unconditional

|25| Proposed Classification:

☐ (R) Restricted ☐ (G) General

|30| Final Classification:

☐ (R) Restricted ☐ (N) Not Classified

|35| Date on Application: 04/12/02 (MO/DAY/YR)

|04| EPA Received Date: 05/02/02 (MO/DAY/YR)

|40| Date Received by PM: 05/21/00 (MO/DAY/YR)

|80| Method of Support:

☐ (1) Cite-All ☐ (6) Owner Submission

☐ (4) Not Applicable ☐ (7) Total Submission

☐ (5) Not Submitted ☐ (8) Selective Method

Reviewers Requested:	DATE SENT	DUE DATE	DATE RETURNED	RESPONSE CODE	RESPONSE DATE
CH					
EF					
PL					
DEB					
NDEB					
TB					
EEB					
EFGB					

|115| FINAL ACTION Response Code 38

|120| Response 05/20/02 (MO/DAY/YR)

75-DAY RESPONSE DUE DATE: ☐ (Y) Yes ☐ (N) No

****
NEW CHEMICAL/FIRST FOOD USE SCREEN
****

1. FILE SYMBOL/REG NO. (ISB) 4383-ET
2. TOLERANCE PETITION NO. (RSB) _____
3. CHEMICAL NAME (RSB) 5-Pyrrolidine-3-carbonitrile, 4-bromo-a-(2-chlorophenyl)-5-(4-fluorophenyl)
4. PESTICIDE CHEMICAL CODE (RSB) 119093
5. PRODUCT NAME (ISB) ECONEA Technical
6. PM (ISB) 33 7. PM TEAM REVIEWER (PM) _____
8. DATE OF RECEIPT (ISB) 5/2/02
9. USE PATTERN (PM) _____
0. DATE OF TRANSMISSION TO PM (ISB) _____
(EPA Receipt Date plus 3 days)
1. DATE OF TRANSMISSION TO HED/EFED/RSB (PM) _____
(PM Receipt Date plus 5 days)
2. HED/EFED/RSB DUE DATE FOR COMPLETION OF SCREEN _____
(HED/EFED Receipt Date plus 10 days)
3. HED/EFED/RSB REVIEWERS:

HED:
TB _____
DEB _____
OREB _____
RD/RSB _____

EFED:
EEB _____
EFGWB _____

4. HED/EFED/RSB COMPLETION DATE (HED) _____ (EFED) _____ (RSB) _____
5. SUBMISSION BARCODE (PM) _____

REGISTRANT PHONE CONTACT INFORMATION (PM)

DATE OF CONTACT _____

PERSON CONTACTED _____

TITLE _____

DECISION & COMMENTS _____

STATUS OF PACKAGE

☐ PASSED SCREEN

☐ FAILED SCREEN (Documentation attached)

CHEMICAL NAME/PESTICIDE CHEMICAL CODE (PCC) REQUEST FORM*

CRA 02-0277

REQUESTOR NAME: Jim Hollins REQUEST DATE: 6/25/02

TEL.: (703) 305-5761 ORG.: IRSD/ESB (DIV./BR./SEC.) ROOM: 232 MAIL CODE: 7506C

CSF ATTACHED:

- [X] YES — If CSF is attached complete Item A and the chemical name in Item B.
- [ ] NO — If CSF is not attached complete Items A through C.

A. INFORMATION REQUIRED:

✓Check Applicable Category

- [ ] Provide PCC and Tolerance Exemption Status For Food-Use Inert Ingredient(s)
- [ ] Provide PCC for Non-Food Use Inert Ingredient (s)
- [X] Provide PCC for Active Ingredient(s)
- [ ] Provide PCC for Dye
- [ ] Determine if Fragrance is Acceptable for Use in Formulation
- [ ] Other (Describe): _____

B. INGREDIENT INFORMATION:

Ingredient No. 1:

Chem. Name: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)

Trade Name:

CAS Reg. No.: 122454-29-9

Ingredient No. 2:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

Ingredient No. 3:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

Ingredient No. 4:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

C. PESTICIDE PRODUCT INFORMATION:

EPA Reg. No./File Symbol: 4383-ET Product Name: ECONEA Technical

Registrant: Janssen Pharmaceutica Food-Use Pesticide: [ ] YES [ ] NO

Percent in Formulation (For Fragrance/Dyes only): _____

INFORMATION REPORTED:

Ingredient No. 1:

PCC: 119093

TOL. STATUS: _____

OTHER INF.: CAS Reg. No. 122454-29-9

Ingredient No. 2:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Ingredient No. 3:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Ingredient No. 4:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Completed By: IRSD/ESB PMN Date Completed: 06/25/2002

*Once completed, this form may be entitled to treatment as CBI under section 10 of FIFRA. If so, a red FIFRA CBI cover should be affixed to the request form and the document handled accordingly.

****
NEW CHEMICAL/FIRST FOOD USE SCREEN
****

1. FILE SYMBOL/REG NO (ISB) 4381 3-ET
2. TOLERANCE PETITION NO. (RSB)
3. CHEMICAL NAME (RSB) Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(ethoxymethyl)
4. PESTICIDE CHEMICAL CODE (RSB) 119093
5. PRODUCT NAME (ISB) ELONEA Technical
6. PM (ISB) 33 7. PM TEAM REVIEWER (PM)
8. DATE OF RECEIPT (ISB) 5/2/02
9. USE PATTERN (PM)
0. DATE OF TRANSMISSION TO PM (ISB)
(EPA Receipt Date plus 3 days)
1. DATE OF TRANSMISSION TO HED/EFED/RSB (PM)
(PM Receipt Date plus 5 days)
2. HED/EFED/RSB DUE DATE FOR COMPLETION OF SCREEN
(HED/EFED Receipt Date plus 10 days)
3. HED/EFED/RSB REVIEWERS:

HED:
TB
DEB
OREB
RD/RSB

EFED:
EEB
EFGWB

4. HED/EFED/RSB COMPLETION DATE (HED) (EFED) (RSB)
5. SUBMISSION BARCODE (PM)

REGISTRANT PHONE CONTACT INFORMATION (PM)

DATE OF CONTACT
PERSON CONTACTED
TITLE
DECISION & COMMENTS

STATUS OF PACKAGE

☐ PASSED SCREEN

☐ FAILED SCREEN (Documentation attached)

CHEMICAL NAME/PESTICIDE CHEMICAL CODE (PCC) REQUEST FORM*

CR#02-0277

REQUESTOR NAME: Jim Hollins REQUEST DATE: 6/25/02

TEL.: (703) 305-5761 ORG.: IRSD/ESB (DIV./BR./SEC.) ROOM: 332 MAIL CODE: 7506C

CSF ATTACHED:

- [X] YES — If CSF is attached complete Item A and the chemical name in Item B.
- [ ] NO — If CSF is not attached complete Items A through C.

A. INFORMATION REQUIRED:

✓Check Applicable Category

- [ ] Provide PCC and Tolerance Exemption Status For Food-Use Inert Ingredient(s)
- [ ] Provide PCC for Non-Food Use Inert Ingredient (s)
- [X] Provide PCC for Active Ingredient(s)
- [ ] Provide PCC for Dye
- [ ] Determine if Fragrance is Acceptable for Use in Formulation
- [ ] Other (Describe): _____

B. INGREDIENT INFORMATION:

Ingredient No. 1:

Chem. Name: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)

Trade Name: [illegible]

CAS Reg. No.: 122454-29-9

Ingredient No. 2:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

Ingredient No. 3:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

Ingredient No. 4:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

C. PESTICIDE PRODUCT INFORMATION:

EPA Reg. No./File Symbol: 4313-ET Product Name: ECONEA Technical

Registrant: Janssen Pharmaceutica Food-Use Pesticide: [ ] YES [ ] NO

Percent In Formulation (For Fragrance/Dyes only): _____

INFORMATION REPORTED:

Ingredient No. 1:

PCC: 119093

TOL. STATUS: _____

OTHER INF.: CAS Reg. No. 122454-29-9

Ingredient No. 2:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Ingredient No. 3:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Ingredient No. 4:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Completed By: LINDA FAIN Date Completed: 06/25/2002

*Once completed, this form may be entitled to treatment as CBI under section 10 of FIFRA. If so, a red FIFI CBI cover should be affixed to the request form and the document [illegible]

****
NEW CHEMICAL/FIRST FOOD USE SCREEN
****

1. FILE SYMBOL/REG NO (ISB) 4381 3-ET -
2. TOLERANCE PETITION NO. (RSB) _____
3. CHEMICAL NAME (RSB) 1H-pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(ethoxymethyl)
4. PESTICIDE CHEMICAL CODE (RSB) 119093
5. PRODUCT NAME (ISB) ELONEA Technical
6. PM (ISB) 33 7. PM TEAM REVIEWER (PM) _____
8. DATE OF RECEIPT (ISB) 5/2/02
9. USE PATTERN (PM) _____
0. DATE OF TRANSMISSION TO PM (ISB) _____ (EPA Receipt Date plus 3 days)
1. DATE OF TRANSMISSION TO HED/EFED/RSB (PM) _____ (PM Receipt Date plus 5 days)
2. HED/EFED/RSB DUE DATE FOR COMPLETION OF SCREEN _____ (HED/EFED Receipt Date plus 10 days)
3. HED/EFED/RSB REVIEWERS:

HED:
TB _____
DEB _____
OREB _____
RD/RSB _____

EFED:
EEB _____
EFGWB _____

4. HED/EFED/RSB COMPLETION DATE (HED) _____ (EFED) _____ (RSB) _____
5. SUBMISSION BARCODE (PM) _____

REGISTRANT PHONE CONTACT INFORMATION (PM)

DATE OF CONTACT _____

PERSON CONTACTED _____

TITLE _____

DECISION & COMMENTS _____

STATUS OF PACKAGE

☐ PASSED SCREEN

☐ FAILED SCREEN (Documentation attached)

CHEMICAL NAME/PESTICIDE CHEMICAL CODE (PCC) REQUEST FORM*

CRC 02-0277

REQUESTOR NAME: Jim Hollins REQUEST DATE: 6/25/02
TEL.: (703) 305-5761 ORG.: IRSD/ESB (DIV./BR./SEC.) ROOM: 222 MAIL CODE: 7506C

CSF ATTACHED:
- [X] YES If CSF is attached complete Item A and the chemical name in Item B.
- [ ] NO If CSF is not attached complete Items A through C.

A. INFORMATION REQUIRED:
(Check Applicable Category)
- [ ] Provide PCC and Tolerance Exemption Status For Food-Use Inert Ingredient(s)
- [ ] Provide PCC for Non-Food Use Inert Ingredient (s)
- [X] Provide PCC for Active Ingredient(s)
- [ ] Provide PCC for Dye
- [ ] Determine if Fragrance is Acceptable for Use in Formulation
- [ ] Other (Describe): _____

B. INGREDIENT INFORMATION:

Ingredient No. 1:
Chem. Name: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)
Trade Name:
CAS Reg. No.: 122454-29-9

Ingredient No. 2:
Chem. Name:
Trade Name:
CAS Reg. No.:

Ingredient No. 3:
Chem. Name:
Trade Name:
CAS Reg. No.:

Ingredient No. 4:
Chem. Name:
Trade Name:
CAS Reg. No.:

C. PESTICIDE PRODUCT INFORMATION:

EPA Reg. No./File Symbol: 4387-ET Product Name: ECONEA Technical
Registrant: Janssen Pharmaceutica Food-Use Pesticide: [ ] YES [ ] NO
Percent in Formulation (For Fragrance/Dyes only):

INFORMATION REPORTED:

Ingredient No. 1:
PCC: 119093
TOL. STATUS:
OTHER INF.: CAS Reg. No. 122454-29-9

Ingredient No. 2:
PCC:
TOL. STATUS:
OTHER INF.:

Ingredient No. 3:
PCC:
TOL. STATUS:
OTHER INF.:

Ingredient No. 4:
PCC:
TOL. STATUS:
OTHER INF.:

Completed By: LINDA FAIN Date Completed: 06/25/2002

*Once completed, this form may be entitled to treatment as CBI under section 10 of FIFRA. If so, a red FIFRA CBI cover should be affixed to the request form and the document [illegible]

****
NEW CHEMICAL/FIRST FOOD USE SCREEN
****

1. FILE SYMBOL/REG NO (ISB) 4381 3-ET -
2. TOLERANCE PETITION NO. (RSB) _____
3. CHEMICAL NAME (RSB) Pyrrole-3-carbonitrile, 4-bromo-2-(2-chlorophenyl)-5-(4-fluorophenyl)
4. PESTICIDE CHEMICAL CODE. (RSB) 119093
5. PRODUCT NAME (ISB) ECONEA Technical
6. PM (ISB) 33 7. PM TEAM REVIEWER (PM) _____
8. DATE OF RECEIPT (ISB) 5/2/02
9. USE PATTERN (PM) _____
0. DATE OF TRANSMISSION TO PM (ISB) _____
(EPA Receipt Date plus 3 days)
1. DATE OF TRANSMISSION TO HED/EFED/RSB (PM) _____
(PM Receipt Date plus 5 days)
2. HED/EFED/RSB DUE DATE FOR COMPLETION OF SCREEN _____
(HED/EFED Receipt Date plus 10 days)
3. HED/EFED/RSB REVIEWERS:

HED:
TB _____
DEB _____
OREB _____
RD/RSB _____

EFED:
EEB _____
EFGWB _____

4. HED/EFED/RSB COMPLETION DATE (HED) _____ (EFED) _____ (RSB) _____
5. SUBMISSION BARCODE (PM) _____

REGISTRANT PHONE CONTACT INFORMATION (PM)

DATE OF CONTACT _____

PERSON CONTACTED _____

TITLE _____

DECISION & COMMENTS _____

STATUS OF PACKAGE

☐ PASSED SCREEN

☐ FAILED SCREEN (Documentation attached)

CHEMICAL NAME/PESTICIDE CHEMICAL CODE (PCC) REQUEST FORM*

CRA# 02-0277

REQUESTOR NAME: Jim Hollins REQUEST DATE: 6/25/02

TEL.: (703) 305-5761 ORG.: ERSD/ESB (DIV./BR./SEC.) ROOM: 232 MAIL CODE: 7506C

CSF ATTACHED:

- [X] YES — If CSF is attached complete Item A and the chemical name in Item B.
- [ ] NO — If CSF is not attached complete Items A through C.

A. INFORMATION REQUIRED:

✓Check Applicable Category

- [ ] Provide PCC and Tolerance Exemption Status For Food-Use Inert Ingredient(s)
- [ ] Provide PCC for Non-Food Use Inert Ingredient (s)
- [X] Provide PCC for Active Ingredient(s)
- [ ] Provide PCC for Dye
- [ ] Determine if Fragrance is Acceptable for Use in Formulation
- [ ] Other (Describe): _____

B. INGREDIENT INFORMATION:

Ingredient No. 1:

Chem. Name: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)

Trade Name:

CAS Reg. No.: 122454-29-9

Ingredient No. 2:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

Ingredient No. 3:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

Ingredient No. 4:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

C. PESTICIDE PRODUCT INFORMATION:

EPA Reg. No./File Symbol: 4313-ET Product Name: ECONEA Technical

Registrant: Janssen Pharmaceutica Food-Use Pesticide: [ ] YES [ ] NO

Percent in Formulation (For Fragrance/Dyes only): _____

INFORMATION REPORTED:

Ingredient No. 1:

PCC: 119093

TOL. STATUS:

OTHER INF.: CAS Reg. No. 122454-29-9

Ingredient No. 2:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Ingredient No. 3:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Ingredient No. 4:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Completed By: LENDA FINN Date Completed: 06/25/2002

*Once completed, this form may be entitled to treatment as CBI under section 10 of FIFRA. If so, a red FIFI CBI cover should be affixed to the request form and the document [illegible]

****
NEW CHEMICAL/FIRST FOOD USE SCREEN
****

1. FILE SYMBOL/REG NO (ISB) 4381 3-ET -
2. TOLERANCE PETITION NO. (RSB) _____
3. CHEMICAL NAME (RSB) 1-methyl-3-carbonitrile, 4-bromo-2-(2-chlorophenyl)-5-(trifluoromethyl)
4. PESTICIDE CHEMICAL CODE (RSB) 119093
5. PRODUCT NAME (ISB) ELONEA Technical
6. PM (ISB) 33 7. PM TEAM REVIEWER (PM) _____
8. DATE OF RECEIPT (ISB) 5/2/02
9. USE PATTERN (PM) _____
0. DATE OF TRANSMISSION TO PM (ISB) _____
(EPA Receipt Date plus 3 days)
1. DATE OF TRANSMISSION TO HED/EFED/RSB (PM) _____
(PM Receipt Date plus 5 days)
2. HED/EFED/RSB DUE DATE FOR COMPLETION OF SCREEN _____
(HED/EFED Receipt Date plus 10 days)
3. HED/EFED/RSB REVIEWERS:

HED:
TB _____
DRB _____
ORRB _____
RD/RSB _____

EFED:
RRB _____
EFGWB _____

4. HED/EFED/RSB COMPLETION DATE (HED) _____ (EFED) _____ (RSB) _____
5. SUBMISSION BARCODE (PM) _____

REGISTRANT PHONE CONTACT INFORMATION (PM)

DATE OF CONTACT _____

PERSON CONTACTED _____

TITLE _____

DECISION & COMMENTS _____

STATUS OF PACKAGE

☐ PASSED SCREEN

☐ FAILED SCREEN
(Documentation attached)

CHEMICAL NAME/PESTICIDE CHEMICAL CODE (PCC) REQUEST FORM*

CRC#02-0277

REQUESTOR NAME: Jim Hollins REQUEST DATE: 6/25/02
TEL.: (703) 305-5761 ORG.: 7RSD/ESB (DIV./BR./SEC.) ROOM: 832 MAIL CODE: 7504C

CSF ATTACHED:
- [X] YES If CSF is attached complete Item A and the chemical name in Item B.
- [ ] NO If CSF is not attached complete Items A through C.

A. INFORMATION REQUIRED:

✓Check Applicable Category
- [ ] Provide PCC and Tolerance Exemption Status For Food-Use Inert Ingredient(s)
- [ ] Provide PCC for Non-Food Use Inert Ingredient (s)
- [X] Provide PCC for Active Ingredient(s)
- [ ] Provide PCC for Dye
- [ ] Determine if Fragrance is Acceptable for Use in Formulation
- [ ] Other (Describe): _____

B. INGREDIENT INFORMATION:

Ingredient No. 1:
Chem. Name: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)
Trade Name:
CAS Reg. No.: 122454-29-9

Ingredient No. 2:
Chem. Name:
Trade Name:
CAS Reg. No.:

Ingredient No. 3:
Chem. Name:
Trade Name:
CAS Reg. No.:

Ingredient No. 4:
Chem. Name:
Trade Name:
CAS Reg. No.:

C. PESTICIDE PRODUCT INFORMATION:

EPA Reg. No./File Symbol: 4313-ET Product Name: ECONEA Technical
Registrant: Sankyo Pharmaceutica Food-Use Pesticide: [ ] YES [ ] NO
Percent in Formulation (For Fragrance/Dyes only): _____

INFORMATION REPORTED:

Ingredient No. 1:
PCC: 119093
TOL. STATUS:
OTHER INF.: CAS Reg. No. 122454-29-9

Ingredient No. 2:
PCC:
TOL. STATUS:
OTHER INF.:

Ingredient No. 3:
PCC:
TOL. STATUS:
OTHER INF.:

Ingredient No. 4:
PCC:
TOL. STATUS:
OTHER INF.:

Completed By: LEONARD FAIN Date Completed: 06/25/2002

*Once completed, this form may be entitled to treatment as CBI under section 10 of FIFRA. If so, a red FIFI CBI cover should be affixed to the request form and the document [illegible]

****
NEW CHEMICAL/FIRST FOOD USE SCREEN
****

1. FILE SYMBOL/REG NO (ISB) 4381 3-ET
2. TOLERANCE PETITION NO.(RSB) _____
3. CHEMICAL NAME (RSB) Pyrrole-3-carbonitrile, 4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)
4. PESTICIDE CHEMICAL CODE (RSB) 119093
5. PRODUCT NAME (ISB) FLONEA Technical
6. PM (ISB) 33 7. PM TEAM REVIEWER (PM) _____
8. DATE OF RECEIPT (ISB) 5/2/02
9. USE PATTERN (PM) _____
0. DATE OF TRANSMISSION TO PM (ISB) _____ (EPA Receipt Date plus 3 days)
1. DATE OF TRANSMISSION TO HED/EFED/RSB (PM) _____ (PM Receipt Date plus 3 days)
2. HED/EFED/RSB DUE DATE FOR COMPLETION OF SCREEN _____ (HED/EFED Receipt Date plus 10 days)
3. HED/EFED/RSB REVIEWERS:

HED:
TB _____
DEB _____
ORNB _____
RD/RSB _____

EFED:
EEB _____
EFGWB _____

4. HED/EFED/RSB COMPLETION DATE (HED) _____ (EFED) _____ (RSB) _____
5. SUBMISSION BARCODE (PM) _____

REGISTRANT PHONE CONTACT INFORMATION (PM)

DATE OF CONTACT _____

PERSON CONTACTED _____

TITLE _____

DECISION & COMMENTS _____

STATUS OF PACKAGE

☐ PASSED SCREEN

☐ FAILED SCREEN (Documentation attached)

CHEMICAL NAME/PESTICIDE CHEMICAL CODE (PCC) REQUEST FORM*

CR# 02-0277

REQUESTOR NAME: Jim Hollins REQUEST DATE: 6/25/02

TEL.: (703) 305-5761 ORG.: IRSD/ESB (DIV./BR./SEC.) ROOM: 322 MAIL CODE: 7504C

CSF ATTACHED:

- [X] YES — If CSF is attached complete Item A and the chemical name in Item B.
- [ ] NO — If CSF is not attached complete Items A through C.

A. INFORMATION REQUIRED:

✓Check Applicable Category

- [ ] Provide PCC and Tolerance Exemption Status For Food-Use Inert Ingredient(s)
- [ ] Provide PCC for Non-Food Use Inert Ingredient (s)
- [X] Provide PCC for Active Ingredient(s)
- [ ] Provide PCC for Dye
- [ ] Determine if Fragrance is Acceptable for Use in Formulation
- [ ] Other (Describe): _____

B. INGREDIENT INFORMATION:

Ingredient No. 1:

Chem. Name: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)

Trade Name:

CAS Reg. No.: 122454-29-9

Ingredient No. 2:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

Ingredient No. 3:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

Ingredient No. 4:

Chem. Name: _____

Trade Name: _____

CAS Reg. No.: _____

C. PESTICIDE PRODUCT INFORMATION:

EPA Reg. No./File Symbol: 4313-ET Product Name: ECONEA Technical

Registrant: Janssen Pharmaceutica Food-Use Pesticide: [ ] YES [ ] NO

Percent in Formulation (For Fragrance/Dyes only): _____

INFORMATION REPORTED:

Ingredient No. 1:

PCC: 119093

TOL. STATUS:

OTHER INF.: CAS Reg. No. 122454-29-9

Ingredient No. 2:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Ingredient No. 3:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Ingredient No. 4:

PCC: _____

TOL. STATUS: _____

OTHER INF.: _____

Completed By: LINDA FANN Date Completed: 06/25/2002

*Once completed, this form may be entitled to treatment as CBI under section 10 of FIFRA. If so, a red FIFI CBI cover should be affixed to the request form and the document ha[illegible]

5-9-02

Date: 5-9-02

File Number: 43813-ET

____ **No Data - File Room Make Ready for** _____
(PM or Individual)

__✓__ **Data - File Room Assign Jacket to Shelf**

____ **Rejected - File Room Assign Jacket to Rejected Shelf**

DATE: 5/8/02

PM 33

EPA COMPANY NUMBER 4381-3-ET

EPA REGISTRATION NUMBER
STATUS (For Amendments) Active_____ Cancelled_____

Not in REFS _____

"Me-Too" CITED PRODUCT STATUS Active_____ Cancelled_____

Not in REFS _____

PRAT RECORD CREATED 5/8/02

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

5/08/2002

JANSSEN PHARMACEUTICA, INC., PLANT/MATERIAL PROTECTION
1125 TRENTON-HARBOURTON ROAD
TITUSVILLE, NJ 08560

OFFICE OF
PREVENTION PESTICIDES AND
TOXIC SUBSTANCES

PRODUCT NAME: ECONEA TECHNICAL
COMPANY NAME: JANSSEN PHARMACEUTICA, INC.
OPP IDENTIFICATION NUMBER: 294604
EPA FILE SYMBOL: 43813-ET
EPA RECEIPT DATE: 5/2/02

SUBJECT: RECEIPT OF APPLICATION FOR A NEW REGISTRATION

DEAR REGISTRANT:

The Office of Pesticides Programs has received your application for a new registration and it has passed an administrative screen for completeness.

Please note that this is only a notification of receipt of your application. This is only the first step in the application process, and does NOT constitute approval.

If you have any questions, please contact Marshall Swindell at 703-308-6341.

Sincerely,

Patricia R. Moore

Front End Processing Staff
Information Services Branch
Information Resources & Services Division

N/FT

PD

JANSSEN PHARMACEUTICA INC.

April 25, 2002

Mr. Marshall Swindell
Product Manager Team 33
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

SUBJECT: ECONEA™ Technical (Janssen Code No. R107894)
Application for Registration
Antimicrobial Division Priority Review to Replace TBTO by 2003

Dear Mr. Swindell:

Janssen Pharmaceutica Inc. is making an application for the registration of ECONEA™ Technical for formulation of antifouling treatment products under the general use pattern of aquatic non-crop. The USEPA Antimicrobial Division has indicated to the ACC Biocides Panel that TBTO replacement products for anti-fouling use would be given a priority for AD resources for expedited review.

Janssen is coordinating this submission with the submission by Sigma Coatings USA B.V. for end-use antifouling paints under the NEXXIUM™ brand of coatings. The regulatory contact for Sigma is Mr. Mike Winter [1-800-221-7978 (x247)].

The following administrative documents (1 copy) are provided:

Document	ECONEA Technical
Application for Pesticide Registration	X
Confidential Statement of Formula (CSF)	X
Certification with Respect to Citation of Data (Form 8570-34)	X
Data Support Matrices - Selective Method of Support (Form 8570-35)	X
Letters of Authorization for ECONEA & NEXXIUM from BASF Corporation	X
Specimen Label (6 copies)	X

1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000
us.janssen.com

A certification statement from Inveresk Research, dated April 17, 2002, is attached to this transmittal letter indicating that the pH of the test solution for the primary eye irritation study is < 2. Consistent with Agency guidelines, this study was not performed, and the technical active substance was categorized as corrosive to eyes for labeling.

Studies submitted by reference to the BASF Corporation file (see Letter of Authorization) for EPA Registration No. 241-366 include:

Study Type	MRID
Acute oral toxicity for AC 303,268 (R107894)	43492824
Acute oral toxicity for metabolite CL 322,250	43492826
Acute oral toxicity for metabolite CL 325,195	43492827
Freshwater fish LC50 (Bluegill) for metabolite CL 325,195	44452617
Acute LC50 freshwater invertebrate for metabolite CL 325,195	44452618
Avian oral LD50 for AC303268 (R107894) – Mallard Duck	43492808
Avian oral LD50 for metabolite CL 325,195 – Mallard Duck	44452612
Avian oral LD50 for AC303268 (R107894) – Bobwhite Quail	43492809
Avian oral LD50 for metabolite CL325,195 – Bobwhite Quail	44452611
All subchronic & chronic toxicology, mutagenicity and metabolism studies	See attached BASF data matrix for product registration 241-366

Data Evaluation Records (DERs) have been submitted for all studies submitted by reference to assist the Anti-Microbial Division in their review.

Supporting data included in the ECONEA application are comprised of three (3) copies each of the following reports:

PRODUCT CHEMISTRY (40 CFR 158.155, 160, 162, 167, 170, 175, 180, 190)

Volume 1 Preliminary Analysis and Certification of Ingredient Limits for the Technical Grade of AC 303268, Report No. APBR 1212, February 7, 2002, BASF, OPPTS Draft Guideline 830.1550, 830.1700 & 830.1750.

MRID _____

Volume 2 Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303268: OPPTS 830.1600, "Description of Materials Used to Produce Product" and OPPTS 830.1620, "Description of Product Process, Report No. P-363.01, January 22, 2001, BASF, OPPTS Draft Guideline 830.1600 & 830.1620.

MRID _____

Volume 3 Product Chemistry Data Requirements for the Manufacturing-Use Product, Technical AC 303.268: OPPTS 830.1670, "Description of the Formation of Impurities", Report No. P-364.01, February 5, 2002, BASF, OPPTS Draft Guideline 830.1670.

MRID _____

Volume 4 Validation of the Ion Chromatographic Method M-3417.01 to Assay for Triethylamine (TEA) in the CL 303268 Technical Grade Active Ingredient (TGAI), Report No. APBR 1130, November 3, 2000, BASF, OPPTS Draft Guideline Reference 830.1700.

MRID _____

Volume 5 Validation of HRGC Method M-3467.01 to Assay for CL 312264 and CL 322697 in the Technical Grade of AC 303268, Report No. APBR 1153, February 27, 2001, BASF, OPPTS Draft Guideline Reference 830.1700

MRID _____

Volume 6 Validation of High Performance Liquid Chromatographic Method M-3397.03 to Assay for the Minor Components in CL 303268 Technical Grade Active Ingredient, Report No. APBR 1129, January 30, 2001, BASF, OPPTS Draft Guideline Reference 830.1700.

MRID _____

Volume 7 Validation of the High Performance Liquid Chromatographic Method M-3408 to Assay for CL 303268 in the Technical Grade Active Ingredient (TGAI), Report No. APBR 1109, March 25, 2002, BASF, OPPTS Draft Guideline Reference 830.1700 & 830.1800.

MRID _____

Volume 8 R107894: Determination of the Physico-Chemical Properties (pH, pKa, and EC Tests A4, A6 and A8), Report No. 1073/41-D2141 (Janssen Report No. AGR00301), January 2001, Covance Laboratories Ltd., OPPTS Draft Guideline Reference Series 63 (158.190).

MRID _____

Volume 9 R107894: Determination of Physico-Chemical Properties, Report No. 1073/48-D2149 (Janssen Report No. AGR00351), July 2001, Covance Laboratories Ltd, OPPTS Draft Guideline Reference Series 63 (158.190).

MRID _____

ENVIRONMENTAL FATE (40 CFR 158.290)

Volume 10 Determination of the Hydrolytic Stability of [14C]-R107894, Report No. 15348, December 22, 1997, Inveresk Research, Date Requirement 161-1.

MRID _____

Volume 11 Supplement to Hydrolytic Stability Report No. 15348-Identification of Hydrolytic Degradation Products of [14C]-R107894, Report No. 15365, December 17, 1997, Inveresk Research, Data Requirement 161-1.

MRID _____

Volume 12 The Anaerobic Degradation of [14C]-R107894 in Two Water/Sediment Systems, Report No. 17832, January 12, 2000, Inveresk Research, Data Requirement 162-3.

MRID _____

Volume 13 The Aerobic Degradation of [14C]-R107894 in Two Water/Sediment Systems, Report No. 16787, February 15, 1999, Inveresk Research, Data Requirement 162-4.

MRID _____

Volume 14 Supplement to Report No. 16787-The Aerobic Degradation of R107894 in Two Water/Sediment Systems, Report No. 17802, October 19, 1999. Inveresk Research, Data Requirement 162-4.

MRID _____

Volume 15 Adsorption/Desorption of [14C]-R107894 in Sediments, Report No. 15715, April 7, 1998, Inveresk Research, Data Requirement 163-1.

MRID _____

Volume 16 Adsorption/Desorption of the Hydrolysis Products of [14C]-R107894 in Sediments, Report No. 16693, January 22, 1999, Inveresk Research, Data Requirement 163-1.

MRID _____

Volume 17 Justification for waiver to conduct soil leaching studies with R107894 based on existing data and pesticide assessment guidance, Report No. 13751-6131, December 13, 2001, Springborn Laboratories, Inc., Guideline Reference 163-1.

MRID _____

TOXICOLOGY (40 CFR 158.340)

ACUTE TOXICOLOGY

Volume 18 R107894 Technical Acute Oral Toxicity (Fixed Dose Procedure) Test in Rats, Report No. 19839, Janssen Report No. AGR308, November 20, 2001, Inveresk Research, OPPTS Draft Guideline 870.1100.

MRID _____

Volume 19 R107894 Technical Acute Dermal Toxicity (LD50) Test in Rats, Report No. 19836, Janssen Report No. AGR307, November 20, 2001, Inveresk Research, OPPTS Draft Guideline 870.1200.

MRID _____

Volume 20 R107894 Technical Acute Inhalation Toxicity Study in Rats, Report No. 19794 (Report Amendment), October 12, 2001, Inveresk Research, OPPTS Draft Guideline 870.1300.

MRID _____

Volume 21 R107894 Technical Acute Dermal Irritation Test in Rabbits, Report No. 20682, Janssen Report No. AGR306, January 11, 2002, Inveresk Research, OPPTS Draft Guideline 870.2500.

MRID _____

Volume 22 R107894 Technical Buehler Test in Guinea Pigs for Delayed Skin Sensitization Potential, Report No. 20973, Janssen Report No. AGR304, January 17, 2002, Inveresk Research, OPPTS Draft Guideline 870.2600.

MRID _____

Volume 23 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Acute Oral Toxicity for AC303,630 (R107894), and metabolites CL 322,250 & CL 325,195, Guideline 81-1

MRID _____

SUBCHRONIC TOXICITY

Volume 24 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 82-1 (870.3100), 82-1a (870.3150), 82-1b (870.3150), 82-2 (870-3200), 82-7 (870.6200), Subchronic Toxicity.

MRID _____

CHRONIC TOXICITY

Volume 25 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 83-1b (870.4100), 83-3a (870.3700), 83-3b (870.3700), 83-4 (870.3800), 83-5 (870.4300), Chronic Toxicity.

MRID _____

MUTAGENICITY

Volume 26 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 84-2 (870.5100), 84-2 (870.5300), 84-2 (870.5375), 84-2 (870.5395), 84-2 (870.5550), Mutagenicity.

MRID _____

METABOLISM

Volume 27 Rationale for Bridging Toxicology Database of Chlorfenapyr and R107894 (CL303268) and Data Evaluation Reports Issued to BASF Corporation and Cited in Toxicity Discussions on AC 303630 and AC 303268, Series 85-1 (870.7485), Metabolism.

MRID _____

ECO-TOXICITY (40 CFR 158.490)

Parent Compound R107894

Volume 28 Acute toxicity of R107894 technical fish, *Oncorhynchus mykiss*, Report No. WE-03-220, (Janssen Rpt. No. AGR 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID _____

Volume 29 Acute toxicity of R107894 technical for fish, *Lepomis macrochirus*, Report No. WE-03-227, (Janssen Rpt. No. AGR 294), April 15, 2002, LISEC, OPPTS Draft Guideline No. 850.1075

MRID _____

Volume 30 R107894-Acute Toxicity to Sheepshead Minnow (*Cyprinodon variegatus*) Under Flow-Through Conditions, Report No. 13751.6119 (Janssen Rpt. No. AGR 368), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1075.

MRID _____

Volume 31 Acute toxicity of R107894 technical for *Daphnia magna*, Report No. WE-01-250 (Janssen Rpt. No. AGR 298), December 10, 2001, LISEC, OPPTS Draft Guideline 850.1010

MRID _____

Volume 32 R107894-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6120 (Janssen Rpt. No. AGR 365), December 3, 2001, Springborn Labs, OPPTS Draft Guideline 850.1025.

MRID _____

Volume 33 R107894-Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions, Report No. 13751.6118 (Janssen Rpt. No. AGR 371), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1035.

MRID _____

Volume 34 R107894-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6128 (Janssen Rpt. No. AGR 383), November 6, 2001, Springborn Labs, OPPTS Draft Guideline 850.1400

MRID _____

Volume 35 *Daphnia magna* reproduction test of R107894 technical, Report No. WE-02-051, (Janssen Rpt. No. AGR 292), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID _____

Volume 36 R107894-Life-Cycle Toxicity Test with Mysids *(Americamysis bahia)*, Report No. 13751.6107 (Janssen Rpt. No. AGR336), July 9, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1350

MRID _____

Volume 37 R107894-Toxicity to Amphipods *(Hyalella azteca)* During a 10-Day Sediment Exposure, Report No. 13751.6105 (Janssen Rpt. No. AGR 340), July 5, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID _____

Volume 38 R107894-Toxicity to Marine Amphipods *(Leptocheirus plumulosus)* During a 10-Day Sediment Exposure, Report No. 13751.6106 (Janssen Rpt. No. AGR 332), July 6, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID _____

Volume 39 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Satisfying Avian LD50 Data Requirements for Mallard Ducks and Bobwhite Quail for AC303,630 (R107894 and Metabolite CL 325,195), Guideline 71-1

MRID _____

Metabolite CL 325,195

Volume 40 Acute toxicity of CL 325,195 for fish, *Oncorhynchus mykiss*, Report No. WE-03-219, (Janssen Rpt. No. AGR 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID _____

Volume 41 CL 325,195 - Acute Toxicity to Sheepshead Minnow (Cyprinodon variegatus) Under Flow-Through Conditions, Report No. 13751.6125 (Janssen Rpt. No. AGR 366), December 10, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1075.

MRID _____

Volume 42 CL325,195-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6126 (Janssen Rpt. No. AGR363), December 13, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1025.

MRID _____

Volume 43 CL325,195-Acute Toxicity to Mysids (Americamysis bahia) Under Flow-Through Conditions, Report No. 13751.6124 (Janssen Rpt. No. AGR 369), November 20, 2001, Springborn Laboratories, FIFRA Guideline Reference Number 72-3, OPPTS Draft Guideline 850.1035.

MRID _____

Volume 44 Fish, Early-life Stage Toxicity Test of CL 325,195 *(Danio rerio)*, Report No. WE-05-003 (Janssen Rpt. No. AGR 290), February 22, 2002, LISEC, OPPTS Draft Guideline 850.1400.

MRID _____

Volume 45 CL 325,195-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6130 (Janssen Rpt. No. AGR384), December 13, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1400

MRID _____

Volume 46 *Daphnia magna* reproduction test of CL 325,195, Report No. WE-02-050 (Janssen Rpt. No. AGR292), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID _____

Volume 47 CL 325,195-Toxicity to Amphipods *(Hyalella azteca)* During a 10-Day Sediment Exposure, Report No. 13751.6116 (Janssen Rpt. No. AGR 343), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID _____

Volume 48 CL 325,195-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6117 (Janssen Rpt. No. AGR 335), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID _____

Volume 49 Data Evaluation Reports Issued to BASF Corporation and Cited by Janssen Pharmaceutica Inc. for Satisfying Aquatic Acute LC50 Toxicity Data Requirements for Bluegill and *Daphnia magna* for Metabolite CL325,195, Guideline 72-1 & 72-2

MRID _____

Metabolite CL 322,250

Volume 50 Acute toxicity of CL 322,250 for fish, *Oncorhynchus mykiss*, Report No. WE-03-221 (Janssen Rpt. No. 296), January 9, 2002, LISEC, OPPTS Draft Guideline 850.1075.

MRID _____

Volume 51 Acute toxicity of CL 322,250 for fish, *Lepomis macrochirus*, Report No. WE-03-228 (Janssen Rpt. No. AGR294), February 15, 2002, LISEC. OPPTS Draft Guideline 850.1075

MRID _____

Volume 52 CL 322,250 - Acute Toxicity to Sheepshead Minnow (Cyprinodon variegatus) Under Flow-Through Conditions, Report No. 13751.6122 (Janssen Rpt. No. AGR 367), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1075.

MRID _____

Volume 53 Acute toxicity of CL 322,250 for *Daphnia magna*, Report No. WE-01-251 (Janssen Rpt. No. AGR 298), December 7, 2001, LISEC, OPPTS Draft Guideline 850.1010

MRID _____

Volume 54 CL322,250-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions, Report No. 13751.6123 (Janssen Rpt. No. AGR 364), December 10, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1025.

MRID _____

Volume 55 CL 322,250 - Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions, Report No. 13751.6121 (Janssen Rpt. No. AGR 370), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1035.

MRID _____

Volume 56 Fish, Early-life Stage Toxicity Test of CL 322,250 *(Danio rerio)*, Report No. WE-05-005 (Janssen Report No. AGR 290), February 22, 2002, LISEC, OPPTS Draft Guideline 850.1400.

MRID _____

Volume 57 CL 322,250-Early Life-Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), Report No. 13751.6129 (Janssen Rpt. No. AGR 385), November 6, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1400

MRID _____

Volume 58 *Daphnia magna* reproduction test of CL 322,250, Report No. WE-02-052, (Janssen Rpt. No. AGR 292), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID _____

Volume 59 CL 322,250-Toxicity to Amphipods (*Hyalella azateca*) During a 10-Day Sediment Exposure, Report No. 13751.6109 (Janssen Rpt. No. AGR 341), October 16, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID _____

Volume 60 CL 322,250 - Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6110 (Janssen Rpt. No. AGR 333), October 18, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID _____

Metabolite CL 322,248

Volume 61 Acute toxicity of CL 322,248 for fish, *Oncorhynchus mykiss*, Report No. WE-03-223, (Janssen Rpt. No. AGR296), December 10, 2001, LISEC, OPPTS Draft Guideline 850.1075

MRID _____

Volume 62 Acute toxicity of CL 322,248 for fish, *Lepomis machrochirus*, Report No. WE-03-229, (Janssen Rpt. No. AGR294), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1075

MRID _____

Volume 63 Acute toxicity of CL 322,248 for *Daphnia magna*, Report No. WE-01-263, (Janssen Rpt. No. AGR 298), April 15, 2002, LISEC, OPPTS Draft Guideline 850.1010

MRID _____

Volume 64 *Daphnia magna* reproduction test of CL 322,248, Report No. WE-02-054 (Janssen Rpt. No. AGR 292), February 15, 2002, LISEC, OPPTS Draft Guideline 850.1300

MRID _____

Volume 65 CL 322,248 - Toxicity to Amphipods (*Hyalella azateca*) During a 10-Day Sediment Exposure, Report No. 13751.6112 (Janssen Rpt. No. AGR 342), October 11, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1735.

MRID _____

Volume 66 CL 322,248-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, Report No. 13751.6113 (Janssen Rpt. No. AGR 334), October 11, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.1740.

MRID _____

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Parent Compound R107894

Volume 67 R107894-Determination of Effects on Seedling Emergence of Rice (*Oryza sativa*), Report No. 13751.6127 (Janssen Rpt. No. AGR362), October 23, 2001, Springborn Labs, OPPTS Draft Guidelines 850.4100 and 850.4225.

MRID _____

Volume 68 R107894-Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6104, (Janssen Rpt. No. AGR 337), April 24, 2001,Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID _____

Volume 69 Alga, growth inhibition test effect of R107894 technical on the growth of *Raphidocelis subcapitata*, Report No. WE-06-261 (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID _____

Volume 70 Alga, growth inhibition test effect of R107894 technical on the growth of *Skeletonema costatum*, Report No. WE-06-270 (Janssen Rpt. No. AGR 307), April 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID _____

Metabolite CL 325,195

Volume 71 CL 325,195 - Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6115 (Janssen Rpt. No. AGR 344), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID _____

Volume 72 Alga, growth inhibition test effect of CL 325,195 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-260, (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID _____

Volume 73 Alga, growth inhibition test effect of CL 325,195 on the growth of *Skeletonema costatum*, Report No. WE-06-269,(Janssen Rpt. No. AGR 309), February 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID _____

Metabolite CL 322,250

Volume 74 CL 322,250-Toxicity to Duckweed, *Lemna gibba*, Report No. 13751.6108 (Janssen Rpt. No. AGR 338), October 12, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID _____

Volume 75 Alga, growth inhibition test effect of CL 322,250 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-262 (Janssen Report No. AGR 300), February 22, 2002, LISEC, OPPTS Draft Guideline 850.5400.

MRID _____

Volume 76 Alga, growth inhibition test effect of CL 322,250 on the growth of *Skeletonema costatum*, Report No. WE-06-271, (Janssen Rpt. No. 309), February 15, 2002, LISEC, OPPTS Data Guideline 850.5400

MRID _____

Metabolite CL 322,248

Volume 77 CL 322,248 - Toxicity to Duckweed, *Lemna gibba* Report No. 13751.6111 (Janssen Rpt. No. AGR 339), October 23, 2001, Springborn Laboratories, OPPTS Draft Guideline 850.4400.

MRID _____

Volume 78 Alga, growth inhibition test effect of CL 322,248 on the growth of *Raphidocelis subcapitata*, Report No. WE-06-266 (Janssen Rpt. No. AGR 300), February 22, 2002, LISEC, OPPTS Data Guideline 850.5400.

MRID _____

Volume 79 Alga, growth inhibition test effect of CL 322,248 on the growth of *Skeletonema costatum*, Report No. WE-06-272, (Janssen Rpt. No. AGR 309), February 15, 2002, LISEC, OPPTS Draft Guideline 850.5400

MRID _____

OCCUPATIONAL EXPOSURE

Volume 80 Screening level occupational exposure assessments for R107894 (CL303268) as an anti-foulant in paint applied to underwater hulls, EXP Project No. 47101, EXP Report No. 02001, January 11, 2002, EXP Corporation, OPPTS Draft Guideline Series 875.

MRID _____

Please consider assigning priority review status to this action since it satisfies the criteria as a TBTO replacement for anti-fouling use; TBTO will no longer be allowed by the International Maritime Organization (IMO) after 2003. The USEPA Antimicrobial Division has identified TBTO anti-fouling replacement products as a priority for receiving a high level of EPA resources in 2002-03 work plan.

Please contact me directly on any matters relating to this registration application. I can be reached by phone at 609-730-2607.

Sincerely,

Bill Goodwine

William R. Goodwine
Director
Plant & Material Protection Division

- NIFT.

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 2-28-95

United States
Environmental Protection Agency
Washington, DC 20460

☑ Registration
☐ Amendment
☐ Other

OPP Identifier Number: 2946-04

Application for Pesticide - Section I

1. Company/Product Number: 43813-ET
2. EPA Product Manager: Marshall Swindell
3. Proposed Classification: ☑ None ☐ Restricted
4. Company/Product (Name): ECONEA Technical
PM#: 33
5. Name and Address of Applicant *(Include ZIP Code)*:
Janssen Pharmaceutica Inc.,Plant/Material Protection
1125 Trenton-Harbourton Road,
Titusville, NJ 08560
☐ *Check if this is a new address*
6. **Expedited Reviw.** In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:
EPA Reg. No. _____
Product Name _____

Section - II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification - Explain below.
☐ Final printed labels in repsonse to Agency letter dated _____
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes ☑ No	☐ Yes ☑ No	☐ Yes ☑ No	☐ Metal ☐ Plastic ☐ Glass ☐ Paper ☑ Other (Specify) Fiber drum
Certification must be submitted	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information: ☑ Label ☐ Container
4. Size(s) Retail Container: 110 lbs (50 kg)
5. Location of Label Directions: ☑ On label
6. Manner in Which Label is Affixed to Product: ☑ Lithograph Paper glued Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
William R. Goodwine	Director	609-730-2607

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowlingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

2. Signature: William R. Goodwine
3. Title: Director
4. Typed Name: William R. Goodwine
5. Date: April 12, 2002
6. Date Application Received (Stamped)

EPA Form 8570-1 (Rev. 3-84) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 2-28-95

EPA

United States
Environmental Protection Agency
Washington, DC 20460

☑ Registration
☐ Amendment
☐ Other

OPP Identifier Number: 294604

Application for Pesticide - Section I

1. Company/Product Number: 43813-

2. EPA Product Manager: Marshall Swindell

3. Proposed Classification: ☑ None ☐ Restricted

4. Company/Product (Name): ECONEA Technical

PM#: 33

5. Name and Address of Applicant *(Include ZIP Code)*:
Janssen Pharmaceutica Inc.,Plant/Material Protection
1125 Trenton-Harbourton Road,
Titusville, NJ 08560
☐ *Check if this is a new address*

6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(ii), my product is similar or identical in composition and labeling to:
EPA Reg. No. _____
Product Name _____

Section - II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes ☑ No	☐ Yes ☑ No	☐ Yes ☑ No	☐ Metal ☐ Plastic ☐ Glass ☐ Paper ☑ Other (Specify) Fiber drum
If "Yes" Certification must be submitted	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information: ☑ Label ☐ Container

4. Size(s) Retail Container: 110 lbs (50 kg)

5. Location of Label Directions: ☑ On label

6. Manner In Which Label Is Affixed to Product: ☑ Lithograph Paper glued Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
William R. Goodwine	Director	609-730-2607

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

2. Signature: William R. Goodwine

3. Title: Director

4. Typed Name: William R. Goodwine

5. Date: April 12, 2002

6. Date Application Received (Stamped)

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060

EPA

United States
Environmental Protection Agency
Washington, DC 20460

☐ Registration
☐ Amendment
☐ Other

OPP Identifier Number
294604

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification ☐ None ☐ Restricted
4. Company/Product (Name)	PM#	

5. Name and Address of Applicant *(Include ZIP Code)*

☐ *Check if this is a new address*

6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section - II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Metal ☐ Plastic ☐ Glass ☐ Paper ☐ Other (Specify)
Certification must be submitted	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information ☐ Label ☐ Container

4. Size(s) Retail Container

5. Location of Label Directions ☐ On Label ☐ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title
4. Typed Name	5. Date

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

PAPERWORK REDUCTION ACT NOTICE and INSTRUCTIONS

PAPERWORK REDUCTION ACT NOTICE: Public reporting burden for this collection of information is estimated to average 0.85 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, (2136), U.S. Environmental Protection Agency, 401 M Street, SW, Washington, DC 20460.

INSTRUCTIONS: This form is to be used for all applications for new registration, and use reregistration, amendment, resubmission, to applications for notifications, final printed labeling, reregistration, etc. In order to process an application for a new registration submitted on this form, the following material must accompany the application:

1. Certification with Respect to Citation of Data (EPA Form 8570-29). (If not exempted by 40 CFR 152.81 (b) (4));
2. Confidential Statement of Formula (EPA Form 8570-4);
3. Formulator's Exemption Statement (EPA Form 8570-27);
4. Five copies of draft labeling;
5. Three copies of any data submitted;
6. Authorization letter where applicable;
7. Metrices where applicable.

Submission of Labeling - Labeling should first be submitted in the form of draft labels with all applications for new registration. Such draft labels may be in the form of typed label text on 8.5 x 11 inch paper for submission or a mockup of the proposed label. If prepared for mockup, it should be constructed in a way as to facilitate storage in an 8.5 x 11 inch file. Mockup labels significantly smaller than 8.5 x 11 inches should be mounted on 8.5 x 11 inch paper for submission.
Submission of Data - Data submitted in support of this application must be submitted in accordance with PR Notice 86-5.

SPECIFIC INSTRUCTIONS: Please read the instructions listed below before completing this application. First determine the type of registration action, listed in Block A, for which you are submitting this application. For applications submitted in connection with New Registration actions, Sections I, III, and IV must be completed by the applicant. For applications submitted in connection with amended reregistration actions, resubmissions, notifications, reregistrations, etc., Sections I, II, and IV must be completed by the applicant.
Block A - Check the appropriate action for which you are submitting this form.

SECTION I - This section must be completed, as applicable, for all registration actions.

1. Company/Product Number - Insert your Company Number, if one has been assigned by EPA. This number may have been assigned to you as a basic registrant, a distributor, or as an establishment. If your product is registered, insert the Product Number.
2. EPA Product Manager - If known, fill in the name and PM number of the EPA Product Manager.
3. Proposed Classification - Specify the proposed classification of this product.
4. Product Name - Enter the complete product name of this pesticide as it will appear on the label. The name must be specific to this product only. Duplication of names is not permitted among products of the same company. Do not include any brand name or company line designations.
5. Name and Address of Applicant - The name of the firm or person and address shown in your application is the person or firm to whom the registration will be issued. If you are acting in behalf of another party, you must submit authorization from that party to act for them in registration matters. An applicant not residing in the United States must have an authorized agent residing in the United States to act for them in all registration matters. The name and complete mailing address of such an agent must accompany this application.
6. Expedited Review - FIFRA section 3 (c) 3 (B) provides for expedited review of applications for registration, or amendments to existing registrations that are similar or identical to other pesticide products that are currently registered with the EPA. In order for your application to be eligible for expedited review, you must provide us with the EPA Registration Number and product name of the product you believe is similar to or identical to your product. The product must be similar or identical in both formulation and labeled uses.

SECTION II - This section must be completed for all applications submitted to amend the registration only of a currently registered product (Amendment), for a resubmission in response to an Agency letter, for notifications to the Agency, for the submission of final printed labeling, for reregistration and for any other action that pertains to a specific EPA-registered product. This section is not to be used for a new application for registration.

1. Subject of submission - Check the applicable block and provide the Agency letter date if appropriate. Provide a brief explanation of the purpose(s) for the submission, such as "the addition of a site, pest or crop (specify)"; "amend the Confidential Statement of Formula by..."; "reregistration submission"; "general label revision of use directions." Attach a separate page if additional space is needed.

SECTION III (Packaging and Container Information) - This Section must be completed for all applications submitted in connection with new registration or applicable amendments.

1. Type of Packaging - Check the appropriate block if your product will be packaged in the indicated packaging types. Indicate the size of the individual packets and number per retail container.
2. Type of Retail Container - Indicate type of container in which product will be marketed.
3. Location of Net Contents - Indicate the location of the net contents information for your product.
4. Size(s) of Retail Container - Specify the net contents of all retail containers for your product.
5. Location of Use Directions - Indicate the location of the use directions for your product.
6. Manner in which label is affixed to product - Indicated the method product label is attached to retail container.

SECTION IV (Contact Point) - This Section must be completed for all applications for Registration actions, i.e., new products registration, resubmission, "me-too," reregistration, etc.

1-5. Self-explanatory.
6. EPA Use Only.

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060

United States
Environmental Protection Agency
Washington, DC 20460

☐ Registration
☐ Amendment
☐ Other

OPP Identifier Number: 294604

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
4. Company/Product (Name)	PM#	☐ None ☐ Restricted

5. Name and Address of Applicant *(Include ZIP Code)*

☐ *Check if this is a new address*

6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section - II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Metal ☐ Plastic ☐ Glass ☐ Paper ☐ Other (Specify)
Certification must be submitted	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ Container		☐ On Label ☐ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product: ☐ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

2. Signature	3. Title	6. Date Application Received (Stamped)
4. Typed Name	5. Date	

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

PAPERWORK REDUCTION ACT NOTICE and INSTRUCTIONS

PAPERWORK REDUCTION ACT NOTICE: Public reporting burden for this collection of information is estimated to average 0.85 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, (2136), U.S. Environmental Protection Agency, 401 M Street, SW, Washington, DC 20460.

INSTRUCTIONS: This form is to be used for all applications for new registration, and use reregistration, amendment, resubmission, to applications for notifications, final printed labeling, reregistration, etc. In order to process an application for a new registration submitted on this form, the following material must accompany the application:

1. Certification with Respect to Citation of Data (EPA Form 8570-29). [If not exempted by 40 CFR 152.81 (b) (4)];
2. Confidential Statement of Formula (EPA Form 8570-4);
3. Formulator's Exemption Statement (EPA Form 8570-27);
4. Five copies of draft labeling;
5. Three copies of any data submitted;
6. Authorization letter where applicable;
7. Matrices where applicable.

Submission of Labeling - Labeling should first be submitted in the form of draft labels with all applications for new registration. Such draft labels may be in the form of typed label text on 8.5 x 11 inch paper for submission or a mockup of the proposed label. If prepared for mockup, it should be constructed in a way as to facilitate storage in an 8.5 x 11 inch file. Mockup labels significantly smaller than 8.5 x 11 inches should be mounted on 8.5 x 11 inch paper for submission.
Submission of Data - Data submitted in support of this application must be submitted in accordance with PR Notice 86-5.

SPECIFIC INSTRUCTIONS: Please read the instructions listed below before completing this application. First determine the type of registration action, listed in Block A, for which you are submitting this application. For applications submitted in connection with New Registration actions, Sections I, III, and IV must be completed by the applicant. For applications submitted in connection with amended reregistration actions, resubmissions, notifications, reregistrations, etc., Sections I, II, and IV must be completed by the applicant.
Block A - Check the appropriate action for which you are submitting this form.

SECTION I - This section must be completed, as applicable, for all registration actions.

1. Company/Product Number - Insert your Company Number, if one has been assigned by EPA. This number may have been assigned to you as a basic registrant, a distributor, or as an establishment. If your product is registered, insert the Product Number.
2. EPA Product Manager - If known, fill in the name and PM number of the EPA Product Manager.
3. Proposed Classification - Specify the proposed classification of this product.
4. Product Name - Enter the complete product name of this pesticide as it will appear on the label. The name must be specific to this product only. Duplication of names is not permitted among products of the same company. Do not include any brand name or company line designations.
5. Name and Address of Applicant - The name of the firm or person and address shown in your application is the person or firm to whom the registration will be issued. If you are acting in behalf of another party, you must submit authorization from that party to act for them in registration matters. An applicant not residing in the United States must have an authorized agent residing in the United States to act for them in all registration matters. The name and complete mailing address of such an agent must accompany this application.
6. Expedited Review - FIFRA section 3 (c) 3 (B) provides for expedited review of applications for registration, or amendments to existing registrations that are similar or identical to other pesticide products that are currently registered with the EPA. In order for your application to be eligible for expedited review, you must provide us with the EPA Registration Number and product name of the product you believe is similar to or identical to your product. The product must be similar or identical in both formulation and labeled uses.

SECTION II - This section must be completed for all applications submitted to amend the registration only of a currently registered product (Amendment), for a resubmission in response to an Agency letter, for notifications to the Agency, for the submission of final printed labeling, for reregistration and for any other action that pertains to a specific EPA-registered product. This section is not to be used for a new application for registration.

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SECTION IV (Contact Point) - This Section must be completed for all applications for Registration actions, i.e., new products registration, resubmission, "me-too," reregistration, etc.

1-5. Self-explanatory.
6. EPA Use Only.

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

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Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
Janssen Pharmaceutica, Plant/Material Protection, 1125 Trenton-Harbourton Rd, Titusville NJ 08560	43813-
Active Ingredient(s) and/or representative test compound(s) Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-trifluoromethyl)	**Date** April 12, 2002
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Aquatic Non-crop	**Product Name** ECONEA Technical

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☑ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

(Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements)

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
William R. Goodwine	April 12, 2002	William R. Goodwine, Director

EPA Form 8570-34 (9-97) Electronic and Paper versions available. Submit only Paper version.

BASF Corporation

BASF

Marshall Swindell, Team Leader
PM Team 33
Regulatory Management Branch 1
Antimicrobials Division
Office of Pesticides Programs
U.S. Environmental Protection Agency
Crystal Mall Building No. 2 Room 266A
1921 Jefferson Davis Highway
Arlington VA, 22202

April 10, 2002

Subject: Authorization for Janssen Pharmaceutica Inc for ECONEA Technical

Dear Mr. Swindell

BASF hereby authorizes the Antimicrobial Division of the Office of Pesticide Programs to reference all BASF owned data submitted to support chlorfenapyr, chemical number 129093. This authorization is limited to the support of the registration application for ECONEA Technical, containing R107894 (Pyrrole-3-carbonotrile,4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl), CAS # 122454-29-9. This Authorization is limited to the purpose of formulating antifoulant coatings.

Respectfully Submitted

John J Arthur
Senior Manager Global Regulatory Affairs.

BASF Corporation

BASF

Marshall Swindell, Team Leader
PM Team 33
Regulatory Management Branch 1
Antimicrobials Division
Office of Pesticides Programs
U.S. Environmental Protection Agency
Crystal Mall Building No. 2 Room 266A
1921 Jefferson Davis Highway
Arlington VA, 22202

April 10, 2002

Subject: Authorization for Sigma Coatings USA NEXIUM products

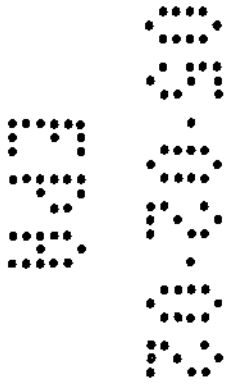
Dear Mr. Swindell

BASF hereby authorizes the Antimicrobial Division of the Office of Pesticide Programs to reference all BASF owned data submitted to support chlorfenapyr, chemical number 129093. This authorization is limited to the support of the registration applications by Sigma Coatings USA for NEXXIUM brand antifouling paints , containing R107894 (Pyrrole-3-carbonitrile,4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl), CAS # 122454-29-9.

Respectfully Submitted,

John J Arthur
Senior Manager Global Regulatory Affairs.

Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com



Inveresk Research
TRANENT EH33 2NE SCOTLAND
TELEPHONE +44 (0) 1875 614548

R107894 Technical
Acute Eye Irritation Test in Rabbits
Inveresk Project No. 577507

The pH of wetted R107894 Technical was determined at Inveresk Research as 1. Current regulatory guidelines recommend that materials which have a result of a pH of less than 2 need not be tested owing to their probable corrosive properties.

The above irritation test was therefore not conducted.

Elizabeth Donald 17 April 2002

Elizabeth Donald
Study Director
Inveresk research

FAX: +44 (0) 1875 614385
E-MAIL: info@inveresk.com
WEBSITE: www.inveresk.com
INVERESK RESEARCH INTERNATIONAL LIMITED
REGISTERED OFFICE ELPHINSTONE RESEARCH CENTRE TRANENT EH33 2NE
REGISTERED IN SCOTLAND NUMBER 91751

JANSSEN PHARMACEUTICA INC.

May 8, 2002

Mr. Marshall Swindell
Product Manager Team 33
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

SUBJECT: ECONEA™ Technical (Janssen Code No. R107894)
Application for Registration – Clarification of BASF Data Matrix
Antimicrobial Division Priority Review to Replace TBTO by 2003

Dear Mr. Swindell:

Janssen Pharmaceutica would like to confirm that we are using the selective method of data support. As such, only pages **14 through 17** of the Chlorfenapyr Technical Insecticide BASF data matrix are being submitted.

Sincerely,

Bill Goodwine

William R. Goodwine
Director
Plant & Material Protection Division
Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

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DATA MATRIX

Date	May 31, 2001	EPA Reg No./File Symbol	241-366	Page 14 of 17

Applicant's/Registrant's Name & Address
BASF Corporation
P.O. Box 400, Princeton, NJ 08543-0400

Product
Chlorfenapyr Technical Insecticide

Ingredient: 4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-trifluoromethyl-1*H*-pyrrole-3-carbonitrile

CAS Reg. No. 122453-73-0

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
SERIES 870	HEALTH EFFECTS TEST GUIDELINES				
870.1100 (81-1)	Acute oral toxicity (rat)	42770207; 42884201	BASF Corporation	OWN	
870.1100 (81-1)	Acute oral toxicity (rat) - metabolites	43492824 43492825 43492826 43492827	BASF Corporation	OWN	
870.1100 (81-1)	Acute oral toxicity (mouse)	43492828	BASF Corporation	OWN	
870.1200 (81-2)	Acute dermal toxicity	42770208	BASF Corporation	OWN	
870.1300 (81-3)	Acute inhalation toxicity: rat	42770209	BASF Corporation	OWN	
870.2400 (81-4)	Acute eye irritation: rabbit	42770210	BASF Corporation	OWN	
870.2500 (81-5)	Acute dermal irritation: rabbit	42770211	BASF Corporation	OWN	
870.2600 (81-6)	Skin sensitization	42770212	BASF Corporation	OWN	
	SUBCHRONIC TOXICITY TEST GUIDELINES				
870.3100 (82-1(a))	90-day oral toxicity in rodents: rat	42770219	BASF Corporation	OWN	
870.3150 (82-1(a))	90-day oral toxicity in rodents: mouse	43492830	BASF Corporation	OWN	

Signature	Name and Title	Date
Dolores A. Chiarello	Dolores A. Chiarello Product Registrations Manager	5/31/01

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DATA MATRIX

Date	May 31, 2001	EPA Reg No./File Symbol	241-366	Page 15 of 17
Applicant's/Registrant's Name & Address	BASF Corporation P.O. Box 400, Princeton, NJ 08543-0400	Product	Chlorfenapyr Technical Insecticide	
Ingredient:	4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-trifluoromethyl-1*H*-pyrrole-3-carbonitrile CAS Reg. No. 122453-73-0			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.3150 (82-1(b))	90-day oral toxicity in nonrodents: dog	42770220	BASF Corporation	OWN	
870.3200 (82-2)	21/28-day dermal toxicity	43492831 43492832	BASF Corporation	OWN	
870.3250 (82-3)	90-day dermal toxicity	–			NA[7]
870.3465 (82-4)	90-day inhalation toxicity	–			NA[7]
	Prenatal developmental toxicity study				
870.3700 (83-3(a))	- rat	42770221; 42884202	BASF Corporation	OWN	
870.3700 (83-3(b))	- rabbit	42770222	BASF Corporation	OWN	
870.3800 (83-4)	Reproduction and fertility effects	43492835; 43492836	BASF Corporation	OWN	
	Chronic Toxicity Test Guidelines				
870.4300 (83-5)	Combined Chronic Toxicity/Carcinogenicity - rat	43492837	BASF Corporation	OWN	
870.4100 (83-1(b))	Chronic Toxicity - dog	43492834	BASF Corporation	OWN	
870.4300 (83-5)	Combined Chronic Toxicity/carcinogenicity - mouse	43492838	BASF Corporation	OWN	
	Genetic Toxicity Test Guidelines				

Signature	Name and Title	Date
Dachiarello	Dolores A. Chiarello Product Registrations Manager	5/31/01

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DATA MATRIX

Date	May 31, 2001	EPA Reg No./File Symbol	241-366	Page 16 of 17

Applicant's/Registrant's Name & Address
BASF Corporation
P.O. Box 400, Princeton, NJ 08543-0400

Product
Chlorfenapyr Technical Insecticide

Ingredient: 4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-trifluoromethyl-1*H*-pyrrole-3-carbonitrile

CAS Reg. No. 122453-73-0

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.5375 (84-2)	In vitro Metaphase chromosomes from CHL Cells	43492839	BASF Corporation	OWN	
870.5140 (84-2)	Gene mulation, Ames test	42770223	BASF Corporation	OWN	
870.5140 (84-2)	Gene mutation, Ames test – metabolites	43492840 43492841 43492842	BASF Corporation	OWN	
870.5375 (84-2)	Structural chromosome aberration test	42770224; 43187601	BASF Corporation	OWN	
870.5395 (84-2)	In vivo mammalian chromosome aberration test – mouse	42770225 43187602	BASF Corporation	OWN	
870.5375 (84-2)	In vitro mammalian chromosome aberration test	43492843	BASF Corporation	OWN	
870.5550 (84-4)	Unscheduled DNA synthesis	42770226	BASF Corporation	OWN	
870.6200 (81-8)	Acute delayed neurotoxicity- rat	43492829; 44067401 44202801	BASF Corporation	OWN	
870.6200 (83-1)	Dietary neurotox – rats	43492833	BASF Corporation	OWN	
	Special Studies Test Guidelines				
870.7485 (85-1)	Metabolism and pharmacokinetics	43492844 44202802	BASF Corporation	OWN	

Signature	Name and Title	Date
D A Chiarello	Dolores A. Chiarello Product Registrations Manager	5/31/01

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DATA MATRIX

Date May 31, 2001	EPA Reg No./File Symbol 241-366	Page 17 of 17
Applicant's/Registrant's Name & Address BASF Corporation P.O. Box 400, Princeton, NJ 08543-0400	**Product** Chlorfenapyr Technical Insecticide	

Ingredient: 4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl)-5-trifluoromethyl-1*H*-pyrrole-3-carbonitrile

CAS Reg. No. 122453-73-0

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
670.7485 (85-1)	Metabolism and pharmacokinetics	43492844 44202802	BASF Corporation	OWN	
	EXPOSURE TEST GUIDELINES				
875.2100 (132-1)	Foliar dissipation – transferable residues				TF
875.2200 (132-1)	Soil dissipation				TF
875.2400 (133-3)	Dermal exposure				TF
875.2500 (133-4)	Inhalation exposure				TF

NA – Not Applicable
NR – Not Required.

1 = Submitted to EPA chemical standards repository on 11/30/93.
2 = Data not required because product contains no combustible liquids. See CFR 40 Part 158.190 footnote 6.
3 = AC 303630 is not an emulsifiable liquid. See 40 CFR Part 158.190 footnote 9.
4 = Not required because product is not a liquid. See CFR 40 Part 158.190 footnote 8.
5 = Not required because the technical is not a liquid at room temperature. See 40 CFR Part 158.190 footnote 2.
6 = No ionizable groups on molecule. Molecule does not dissociate.
7 = Not required for this use.
8 TF = BASF Corporation is a member of the Outdoor Residential Exposure Task Force, the Agricultural Reentry Task Force, and the Spray Drift Task Force.

Signature	Name and Title	Date
DaChiarello	Dolores A. Chiarello Product Registrations Manager	5/31/01

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Form Approved OMB No. 2070-0060

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Product Chemistry

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Draft Guideline 830.1550	Product identity and composition		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1700	Preliminary analysis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1750	Certified limits		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1600	Description of materials used to product the product		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1620	Description of production process		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1670	Discussion of formation of impurities		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1700	Preliminary analysis 1 - impurities		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1700	Preliminary analysis 2 - impurities		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1700	Preliminary analysis 3 - impurities		Janssen Pharmaceutica Inc.	OWN	
OPPTS 830.1700 & 830.1800	Preliminary analysis + Enforcement analytical method		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 63 (158.190)	Physical and chemical characteristics 1		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 63 (158.190)	Physical and chemical characteristics 2		Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	April 22, 2002

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Ingredient R107894 Product Chemistry

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Draft Guideline 830.1550	Product identity and composition		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1700	Preliminary analysis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1750	Certified limits		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1600	Description of materials used to product the product		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1620	Description of production process		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1670	Discussion of formation of impurities		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1700	Preliminary analysis 1 - impurities		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1700	Preliminary analysis 2 - impurities		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 830.1700	Preliminary analysis 3 - impurities		Janssen Pharmaceutica Inc.	OWN	
OPPTS 830.1700 & 830.1800	Preliminary analysis + Enforcemant analytical method		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 63 (158.190)	Physical and chemical characteristics 1		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 63 (158.190)	Physical and chemical characteristics 2		Janssen Pharmaceutica Inc.	OWN	

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Ingredient R107894 Environmental Fate

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Draft Guideline 161-1	Hydrolysis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 161-1	Hydrolysis supplement		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 162-3	Anaerobic aquatic		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 162-4	Aerobic aquatic		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 162-4	Aerobic aquatic supplement		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 163-1	Leaching and adsorption - Hydrolysis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 163-1	Hydrolysis - degradation products		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 163-1	Leaching - waiver request		Janssen Pharmaceutica Inc.	OWN	

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Ingredient R107894 Subchronic Toxicity

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 870.3100 (82-1)	90 day oral toxicity in rodents	42770219	BASF	EXC	
OPPTS Guideline 870.3150 (82-1a)	90 day oral toxicity in nonrodents	43492830	BASF	EXC	
OPPTS Guideline 870.3150 (82-1b)	90 day oral toxicity in nonrodents	42770220	BASF	EXC	
OPPTS Guideline 870.3200 (82-2)	21/28 day dermal toxicity	43492831	BASF	EXC	
OPPTS Guideline 870.6200 (82-7)	Neurotoxicity screening battery	43492833	BASF	EXC	

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107694 Acute Toxicology

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Draft Guideline 870.1100	Acute oral toxicity		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 870.1200	Acute dermal toxicity		Janssan Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 870.1300	Acute inhalation toxicity		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 870.2500	Acute dermal irritation		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 870.2600	Skin sensitization		Janssen Pharmaceutica Inc.	OWN	
OPPTS Draft Guideline 61-1	Acute oral toxicity	43492824	BASF	EXC	
OPPTS Draft Guideline 61-1	Acute oral toxicity	43492826	BASF	EXC	
OPPTS Draft Guideline 81-1	Acute oral toxicity	43492827	BASF	EXC	

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Ingredient R107894 Chronic Toxicity

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 870.4100 (83-1b)	Chronic toxicity	43492834	BASF	EXC	
OPPTS Guideline 870.3700 (83-3a)	Prenatal developmental toxicity study	42884202	BASF	EXC	
OPPTS Guideline 870.3700 (83-3a)	Prenatal developmental toxicity study	42770221	BASF	EXC	
OPPTS Guideline 870.3800 (83-3b)	Prenatal developmental toxicity study	42770222	BASF	EXC	
OPPTS Guideline 870.4300 (83-4)	Reproduction and fertility effects	43492835/36	BASF	EXC	
OPPTS Guideline 870.4300 (83-5)	Combined chronic toxicity/carcinogenicity	43492837	BASF	EXC	

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Ingredient R107894 Mutagenicity

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 870.5100 (84-2)	Bacterial reverse mutation test	42770223	BASF	EXC	
OPPTS Guideline 870.5300 (84-2)	In vitro mammalian cell gene mutation test	42770224	BASF	EXC	
OPPTS Guideline 870.5300 (84-2)	In vitro mammalian cell gene mutation test	43187601	BASF	EXC	
DPPTS Guideline 870.5375 (84-2)	In vitro mammalian chromosome aberration test	43492839	BASF	EXC	
OPPTS Guideline 870.5375 (84-2)	In vitro mammalian chromosome aberration test	43492843	BASF	EXC	
OPPTS Guideline 870.5395 (84-2)	Mammalian erythrocyte micronucleus test	43187602	BASF	EXC	
OPPTS Guideline 870.5395 (84-2)	Mammalian erythrocyte micronucleus test	42770225	BASF	EXC	
OPPTS Guideline 870.5550 (84-2)	Bacterial DNA damage or repair tests	42770226	BASF	EXC	

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Ingredient R107894 Metabolism

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 870.7485 (85-1)	Metabolism and pharmacokinetics	43492844	BASF	EXC	

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Ingredient R107894 Eco-Toxicity - Parent Compound R107894

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.1075	Fish acute toxicity test, freshwater Rainbow Trout		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1075	Fish acute toxicity test, freshwater Bluegill		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1075	Fish acute toxicity test, marine		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1010	Aquatic invertebrate acute tox, test, freshwater daphnids		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1025	Oyster acute toxicity test (shell deposition)		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1035	Mysid acute toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1400	Fish early-life stage toxicity test - marine		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1300	Daphnid chronic toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1350	Mysid chronic toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1735	Whole sediment acute toxicity invertebrates, freshwater		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1740	Whole sediment acute toxicity invertebrates, marine		Janssen Pharmaceutica Inc.	OWN	
Guideline 71-1(a)	Avian single dose LO50 test - Mallard Duck	43492808	BASF	EXC	
Guideline 71-1(a)	Avian single dose LD50 test - Bobwhite Quail	43492809	BASF	EXC	

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Ingredient R107894 Eco-Toxicity - Metabolite CL 325,195

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.1075	Fish acute toxicity test, freshwater Rainbow Trout		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1075	Fish acute toxicity test, marine		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1025	Oyster acute toxicity test (shell deposition)		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1035	Mysid acute toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1400	Fish early-life stage toxicity test - freshwater		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1400	Fish early-life stage toxicity test - marine		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1300	Daphnid chronic toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1735	Whole sediment acute toxicity invertebrates, freshwater		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1740	Whole sediment acute toxicity invertebrates, marine		Janssen Pharmaceutica Inc.	OWN	
Guideline 72-1	Fish toxicity test - freshwater - BlueGill	44452617	BASF	EXC	
Guideline 72-2	Aquatic invertebrate acute tox test, freshwater daphnids	44452618	BASF	EXC	
Guideline 71-1(a)	Avian single dose LD50 Mallard Duck	44452612	BASF	EXC	
Guideline 71-1(a)	Avian single dose LD50 Bobwhite Quail	44452611	BASF	EXC	

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Ingredient R107894 Eco-Toxicity - Metabolite CL 322,250

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.1075	Fish acute toxicity test, freshwater and Rainbow Trout		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1075	Fish acute toxicity test, freshwater and Bluegill		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1075	Fish acute toxicity test, freshwater and marine		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1010	Aquatic invertebrate acute tox test, freshwater daphnids		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1025	Oysler acute toxicity test (shell deposition)		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1035	Mysid acute toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1400	Fish early-life stage toxicity test - freshwater		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1400	Fish early-life stage toxicity test - marine		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1300	Daphnid chronic toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1735	Whole sediment acute toxicity invertebrates, freshwater		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1740	Whole sediment acute toxicity invertebrates, marine		Janssen Pharmaceutica Inc.	OWN	

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Ingredient R107894 Eco-Toxicity - Metabolite CL 322,248

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
DPPTS Guideline 850.1075	Fish acute toxicity test, Rainbow Trout		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 650.1075	Fish acute toxicity test, Bluegill		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1010	Acute invertebrate acute tox, test, freshwater daphnids		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1300	Daphnid chronic toxicity test		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1735	Whole sediment acute toxicity invertebrates, freshwater		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.1740	Whole sediment acute toxicity invertebrates, marine		Janssen Pharmaceutica Inc.	OWN	

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Ingredient R107894 Plant Protection/Non-Target Plants/Parent Compound R107894

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.4100/4225	Terrestrial plant toxicity, Tier 1 (seedling emergence)		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.4400	Aquatic plant tox test using Lemna spp. Tiers I and II		Janssen Pharmaceutica, Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Raphidocalis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Skeletonema		Janssen Pharmaceutica Inc.	OWN	

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Plant Protection/Non-Target Plants/Metabolite CL 325,195

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.4400	Aquatic plant tox1est using Lemna spp. Tiers I and II		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Raphidocelis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Skelatonema		Janssen Pharmaceutica Inc.	OWN	

Signature William R Goodwine	Name and Title William R. Goodwine	Date April 22, 2002

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Plant Protection/Non-Target Plants/Metabolite CL 322,250

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.4400	Aquatic plant tox test using Lemna spp. Tiers I and II		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Raphidocelis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Skeletonema		Janssen Pharmaceutica Inc.	OWN	

Signature William R. Goodwine	Name and Title William R. Goodwine	Date April 22, 2002

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107694 Plant Protection/Non-Target Plants/Metabolite CL 322,248

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Guideline 850.4400	Aquatic plant tox test using Lemna spp. Tiers I and II		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Raphidocelis		Janssen Pharmaceutica Inc.	OWN	
OPPTS Guideline 850.5400	Algal toxicity, Tiers I and II - Skeletonema		Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	April 22, 2002

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Occupational Exposure

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
OPPTS Draft Guideline Series 675	Occupational exposure assessments		Janssen Pharmaceutica Inc.	OWN	

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Product Chemistry

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	April 22, 2002

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Environmental Fate

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	April 22, 2002

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Acute Toxicology

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	

MRID 46220-01

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	April 22, 2002

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Subchronic Toxicity

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	

Signature William R. Goodwins

Name and Title William R. Goodwins

Date April 22, 2002

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Chronic Toxicity

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	

Signature William R. Goodwine

Name and Title William R. Goodwine

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Mutagenicity

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	

Signature	Name and Title	Date
William R. Goodwin	William R. Goodwin	April 22, 2002

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Metabolism

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			BASF	EXC	

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Name and Title: William R. Goodwine

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Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Eco-Toxicity - Parent Compound R107894

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			BASF	EXC	
			BASF	EXC	

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Name and Title
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Date
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Ingredient R107894	Eco-Toxicity - Metabolite CL 325,195				
Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	
			BASF	EXC	

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Ingredient R107894 Eco-Toxicity - Metabolite CL 322,250

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	

Signature William R. Goodwine

Name and Title
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Ingredient R107894 Eco-Toxicity - Metabolite CL 322,248

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	

Signature William R. Goodwine

Name and Title
William R. Goodwine

Date
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Ingredient R107894 Plant Protection/Non-Target Plants/Parent Compound R107894

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica, Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	

Signature	Name and Title	Date
William R. Goodwine	William R. Goodwine	April 22, 2002

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Ingredient R107894 Plant Protection/Non-Target Plants/Metabolite CL 325,195

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	

Signature William R. Goodwine

Name and Title: William R. Goodwine

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Ingredient R107894 Plant Protection/Non-Target Plants/Metabolite CL 322,250

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	

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Ingredient R107894	Plant Protection/Non-Target Plants/Metabolite CL 322,248	

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	
			Janssen Pharmaceutica Inc.	OWN	

N/D

21-21-01

Signature William R. Goodwine	Name and Title William R. Goodwine	Date April 22, 2002

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Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

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DATA MATRIX

Date April 22, 2002	EPA Reg No./File Symbol 43813	Page 16 of 16
Applicant's/Registrant's Name & Address Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200	Product ECONEA Technical	

Ingredient R107894 Occupational Exposure

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Janssen Pharmaceutica Inc.	OWN	

Signature William R. Goodwine

Name and Title: William R. Goodwine

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PRECAUTIONARY STATEMENT
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

DANGER

Fatal if swallowed. Corrosive. Causes irreversible eye damage. Do not get in eyes or on clothing. Wear protective eyewear such as goggles, face shield or safety glasses. Wash thoroughly with soap and water after handling and before eating, drinking, or using tobacco. Harmful if inhaled or absorbed through the skin. Avoid breathing dust. Avoid contact with skin, eyes, or clothing. Remove contaminated clothing and wash clothing before reuse.

FIRST AID	
If swallowed	-Call a poison control center or doctor immediately for treatment advice. -Have person sip a glass of water if able to swallow. -Do not induce vomiting unless told to do so by a poison control center or doctor. -Do not give anything by mouth to an unconscious person.
If in eyes	-Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. -Call a poison control center or doctor for treatment advice.
If inhaled	-Move person to fresh air. -If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. -Call a poison control center or doctor for further treatment advice
If on skin or clothing	-Take off contaminated clothing. -Rinse skin immediately with plenty of water for 15-20 minutes. -Call a poison control center or doctor for treatment advice.

HOT LINE NUMBER:
Chem Trec: (800) 424-9300
Have the product container with you when calling a poison control center or doctor, or going for treatment

NOTE TO PHYSICIAN
Probable mucosal damage may contraindicate the use of gastric lavage.

ECONEA™

Technical

Anti-fouling Preservative

For Formulating Use Only

ACTIVE INGREDIENT: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)	93.2%
INERT INGREDIENTS:	6.8%
TOTAL:	100.0%

KEEP OUT OF REACH OF CHILDREN

DANGER **POISON**

See side panel for first aid and additional precautionary statements.

EPA Reg. No.:43813-XX
EPA Est. No.: 241-MO-001

NET Contents: 110 lbs. (50 kgs)

JANSSEN PHARMACEUTICA
1125 Trenton-Harbourton Road
Titusville, NJ 08560

04/02

DIRECTIONS FOR USE
It is a violation of Federal law to use this product in a manner inconsistent with its labeling.
This product is for formulation into anti-fouling products for control of hard fouling organisms. Each formulator is responsible for obtaining EPA registration for their end-use product(s).

STORAGE AND DISPOSAL
PROHIBITIONS: Do not contaminate water, food or feed by storage and disposal.
STORAGE: DO NOT mix or store this product or solutions of this product in a manner inconsistent with its labeling.
DISPOSAL: Pesticide wastes may be acutely hazardous. Improper disposal is a violation of Federal Law.
PESTICIDE DISPOSAL: Pesticide, mixtures, or equipment rinse waters that cannot be chemically reprocessed must be disposed of according to applicable federal, state or local procedures. Contact your State Pesticide or Environmental Control Agency or the Hazardous Waste representative at the nearest EPA Regional Office for guidance.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into formulation equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If burned, stay out of smoke. If drum is contaminated and cannot be reused, dispose of in the same manner.

ENVIRONMENTAL HAZARDS
Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

NOTICE OF WARRANTY
Janssen Pharmaceutica warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with the directions under normal use conditions. It is impossible to eliminate all risks inherently associated with the use of this product. Ineffectiveness or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of Janssen Pharmaceutica. In no case shall Janssen Pharmaceutica be liable for consequential, special or indirect damages resulting from the use or handling of this product. The Buyer shall assume all such risks. **Janssen Pharmaceutica makes no warranties of merchantability of fitness for a particular purpose or any other express or implied warranty except as stated above.**

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Pages 438-445 - *Confidential Statements of Formula may be entitled to confidential treatment*